Nervous & mental disease
Monogr. # 16

Nervous and Mental Disease Monograph Series No. 16

# ACUTE POLIOMYELITIS

## HEINE-MEDIN'S DISEASE

By

DR. IVAN WICKMAN

Stockholm

New York

1913

## ANNOUNCEMENT

THE Nervous and Mental Disease Monograph Series will consist of short monographs, translations and minor text-books, on subjects related to these specialties. It is purposed to issue them from time to time as the material becomes available. The editors will be pleased to consider the availability of manuscripts for the series.

# Nervous and Mental Disease Monograph Series

Editors

SMITH ELY JELLIFFE, M.D.

WM. A. WHITE, M.D.

No. 1. Outlines of Psychiatry. (Fourth Edition, 1913.) Price, $3.00
By WM. A. WHITE, M.D.

No. 2. Studies in Paranoia. (Out of Print.)

No. 3. Psychology of Dementia Praecox. (Out of Print.)

No. 4. Selected Papers on Hysteria and Other Psychoneuroses. (Second Edition, 1912.) Price, $2.50
By PROF. SIGMUND FREUD, M.D.

No. 5. The Wassermann Serum Reaction in Psychiatry. Price, $2.00
By FELIX PLAUT, M.D.

No. 6. Epidemic Poliomyelitis. (Out of Print.)

No. 7. Three Contributions to Sexual Theory . . . . . Price, $2.00
By PROF. SIGMUND FREUD

No. 8. Mental Mechanisms . . . . . Price, $2.00
By WM. A. WHITE, M.D.

No. 9. Studies in Psychiatry . . . . . Price, $2.00
By Members of the New York Psychiatrical Society

No. 10. Methods of Mental Examination . . . . . Price, $2.00
By SHEPHERD IVORY FRANZ, Ph.D.

No. 11. The Theory of Schizophrenic Negativism . . . . . Price, $ .60
By PROFESSOR E. BLEULER

No. 12. Cerebellar Functions . . . . . Price, $3.00
By DR. ANDRÉ-THOMAS

No. 13. History of the Prison Psychoses . . . . . Price, $1.25
By DRS. P. NITSCHE and K. WILMANNS

No. 14. General Paresis . . . . . Price, $3.00
By PROF. E. KRAEPELIN

No. 15. Dreams and Myths . . . . . Price, $1.00
By DR. KARL ABRAHAM

No. 16. Poliomyelitis . . . . . Price, $3.00
DR. I. WICKMANN

No. 17. Freud's Theories of the Neuroses . . . . . Price, $2.00
DR. E. HITSCHMANN

---

Address all communications to JOURNAL OF NERVOUS AND MENTAL DISEASE
DISEASE, 64 West Fifty-Sixth Street, New York.

NERVOUS AND MENTAL DISEASE MONOGRAPH
SERIES, NO. 16

# ACUTE POLIOMYELITIS

(HEINE-MEDIN'S DISEASE)

BY
DR. IVAN WICKMAN
of Stockholm

Authorized English Translation by
DR. J. WM. J. A. M. MALONEY, F.R.S.Ed.

ILLUSTRATED

NEW YORK
THE JOURNAL OF NERVOUS AND MENTAL DISEASE
PUBLISHING COMPANY
1913

## NERVOUS AND MENTAL DISEASE MONOGRAPH SERIES

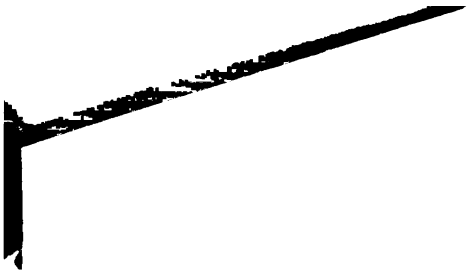
Edited by
Drs. SMITH ELY JELLIFFE and WM. A. WHITE
Numbers Issued

1. Outlines of Psychiatry. (4th Edition.) $3.00.
By Dr. William A. White.
2. Studies in Paranoia.
By Drs. N. Gierlich and M. Friedman.
3. The Psychology of Dementia Praecox. (Out of Print.)
By Dr. C. G. Jung.
4. Selected Papers on Hysteria and other Psychoneuroses.
(2d Edition.) $2.50. By Prof. Sigmund Freud.
5. The Wassermann Serum Diagnosis in Psychiatry. $2.00.
By Dr. Felix Plaut.
6. Epidemic Poliomyelitis. New York, 1907. (Out of Print.)
7. Three Contributions to Sexual Theory. $2.00.
By Prof. Sigmund Freud.
8. Mental Mechanisms. $2.00. By Dr. Wm. A. White.
9. Studies in Psychiatry. $2.00.
New York Psychiatrical Society.
10. Handbook of Mental Examination Methods. $2.00.
By Shepherd Ivory Franz.
11. The Theory of Schizophrenic Negativism. $0.60.
By Professor E. Bleuler.
12. Cerebellar Functions. $3.00.
By Dr. André-Thomas.
13. History of Prison Psychoses. $1.25.
By Drs. P. Nitsche and K. Wilmanns.
14. General Paresis. $3.00. By Prof. E. Kraepelin.
15. Dreams and Myths. $1.00. By Dr. Karl Abraham.
16. Poliomyelitis. $3.00. Dr. I. Wickmann.
17. Freud's Theories of the Neuroses. $2.00.
Dr. E. Hitschmann.



PRESS OF
THE NEW ERA PRINTING COMPANY
LANCASTER, PA

# TABLE OF CONTENTS



# ACUTE POLIOMYELITIS

## HEINE-MEDIN'S DISEASE

---

## CHAPTER I

### INTRODUCTION

*Historical Review.*—Acute poliomyelitis, for many years known as infantile paralysis, has so often of late appeared in epidemic form that our knowledge of it has been considerably amplified. We have learned that acute poliomyelitis is much more protean in its manifestations than was formerly taught. So variable has it shown itself, that even clinicians of wide experience doubt the identity of epidemic infantile paralysis with the classical malady in which only sporadic cases appeared.

Wickman has suggested that all forms of disease arising from the same virus as acute poliomyelitis should be grouped under the one term—Heine-Medin's Disease. This nomenclature has been adopted, especially in Germany and Austria, by many with considerable experience in the recent epidemics.

Infantile paralysis was mentioned first by Underwood at the end of the eighteenth century. The credit of differentiating the disease from more or less similar conditions of cerebral origin belongs to Heine, who in 1840 published his masterly article on this disease. Duchenne, later, demonstrated the behavior of the affected muscles to faradic, and Erb, to galvanic stimulation. Surprisingly little further progress in our clinical knowledge was made until Medin published his celebrated observations on the Stockholm epidemic of 1887. Medin recognized, in addition to the already familiar spinal form, a bulbar, a polyneuritic, an ataxic and an encephalitic type. The last, from theoretical considerations, had previously been foreshadowed by Strümpell and Pierre Marie. The clinical significance of Medin's work re-

mained almost unappreciated until the accumulated evidence from the recent epidemics emphasized its enormous value.

The first of these great epidemics appeared in 1905 almost simultaneously in Norway and Sweden. Wickman fully reported the Swedish epidemic. He distinguished several new types,—a meningitic, an abortive, and a form resembling Landry's paralysis. The basis of Landry's paralysis he found sometimes to be an acute poliomyelitis; but he further noted—what until then had not been recognized—that most fatal cases run a course closely resembling that of a Landry's paralysis. His observations showed that the disease was a general infection with specific localization in the nervous system. Wickman's work was followed by that of Leegaard (1909), upon the Norwegian epidemic of 1905; by that of Zappert and others (1909), upon the Austrian epidemic of 1908; by the report of the American School (1910), upon the New York epidemic of 1907; and by a particularly valuable contribution from Ed. Müller (1910), upon the Hesse-Nassau epidemic of 1909.

Although Prévost and Vulpian, in 1865, had described atrophy of the anterior horn and of the motor ganglion cells in a case of infantile paralysis in which the acute stage of the disease was long passed; and Roger and Damaschino, in 1871, had reported the changes in the stage of recovery; Rissler, in 1885, was the first to give a comprehensive description of the pathologic-anatomical processes of the acute stage. He demonstrated the inflammatory reaction in the blood vessels and also the degeneration in the ganglion cells. Later, isolated cases were reported by Dauber, Goldscheider, Siemerling, Redlich, and others. Wickman, in 1905, published the first work comprising a large series of recent cases. By his, and by the subsequent investigations of Forssner, Sjovall, Harbitz and Scheel, Marburg, Beneke, Strauss and others, the pathological anatomy of the acute stage was conclusively demonstrated to be an acute meningoencephalopoliomyelitis.

Thanks, not only to the researches above mentioned, but also to those of Charcot and Joffroy, Roth, Fr. Schultze, and others, the changes in the chronic stage, however, had then long been known.

The first attempt to explain the morbid process was made by Charcot. He conceived it to be a primary degeneration of the ganglion cells with secondary involvement of the vessels. This was a simple and apparently adequate conception and it conformed

to the clinical picture presented by the malady. Most observers of recent cases—which were just beginning to be recognized—believed the process to be a true inflammation. Some regarded the degeneration of the ganglion cells as a sequel to the inflammation, while others looked upon the degeneration and the inflammation as simultaneous processes. Following the lead of Pierre Marie, most considered that the anterior horns were always affected because of implication of the arteria centralis. Wickman, on the other hand, maintained the lymphatic spread of the disease, and the latest experimental researches confirm the correctness of his opinion.

Very inexact ideas were prevalent concerning the nature of the disease until Strümpell and Pierre Marie, from its general character and its onset with fever, recognized it to be an infection. Their opinion was supported by the fact that infantile paralysis sometimes appeared in epidemics.

The first epidemic of infantile paralysis to be described was that reported by the Swedish physician, Bergenholtz, in 1881. Subsequently, several others were recorded, but most of them consisted of relatively few cases. The most celebrated were those which occurred in 1887 and 1895, in Stockholm. They were reported by Medin. Neither in these, nor in any other outbreak, however, was it possible to ascertain how the disease spread. During the Swedish epidemic of 1905, through the observation of indisputable abortive forms, and through the study of all possible means of communication, Wickman succeeded in proving that Heine-Medin's disease spreads from person to person in exactly the same way as other contagious maladies. This has, in subsequent epidemics, partly been confirmed by Ed. Müller, P. Krause and others.

Although many problems of this malady have been elucidated, many are still unsolved. The cause of the disease is not yet known. Of late years, quite a number of very interesting experimental investigations of poliomyelitis in monkeys have been published and have greatly increased our knowledge of this disease. Landsteiner and Popper were the first successfully to infect monkeys. From the work of Flexner and Lewis, Landsteiner and Prasek, Knöpfelmacher, Leiner and Von Wiesner, Römer, Römer and Joseph, Levaditi and Landsteiner, Netter and Levaditi, and

others, we must conclude that the cause of acute poliomyelitis does not belong to the class of the common bacteria, but is a filterable virus, and is present in the spinal cord.

*Epidemic and Sporadic Acute Poliomyelitis.*—It may not be inappropriate to refer here to the relation between epidemic and acute poliomyelitis. Some assert that both conditions are not identical. The following are the principal reasons for this assertion: (*a*) the clinical picture of Heine-Medin's disease is much more variable than that of the classical infantile paralysis; (*b*) in a number of cases of the former disease the cranial nerves are specially involved, whereas cranial nerve lesions usually do not occur in infantile paralysis; (*c*) adults are more liable to be attacked in epidemic poliomyelitis; (*d*) sporadic poliomyelitis seldom runs a lethal course, whereas the epidemic variety has a considerable mortality; (*e*) and, finally, the epidemic occurrence itself is a characteristic distinction.

The difference in symptomatology is more apparent than real. Obviously very different opportunities for clinical observation exist when hundreds of cases can be examined together than when only isolated cases are available from year to year. In epidemics, connections can be clearly traced between symptom complexes, which in isolated cases may appear unrelated, and the fact must be emphasized that the spinal type (the classical infantile paralysis) forms the nucleus of Heine-Medin's disease. From the most recent observations as to the localization of the paralysis, it is evident that the extremities—especially the legs—are oftenest affected. No doubt of the complete correspondence of the disease with the ancient infantile paralysis can endure. The changes in the acute and chronic stages have been shown to be absolutely identical in both. Netter and Levaditi have procured further and remarkably interesting evidence. They were able to prove in a case of sporadic acute poliomyelitis in which the acute stage had occurred three years previously, that the serum "in vitro" destroyed the virus of the epidemic poliomyelitis.

I wish, nevertheless, to refer here to certain peculiarities of Heine-Medin's disease, and to some circumstances which may explain why the epidemic and the sporadic forms have been regarded as distinct.

Heine-Medin's disease shows a striking variability which is

evident not only in the different epidemics; not only in the various foci of the same epidemic; but also even in the different cases within a single focus. Its protean character may be gathered from the reports of different observers. Thus, one observer sees none but the typical; while another, of mature experience, reports a number of atypical cases. I can refer to no better examples than Medin, Nonne and Spieler, who, according to present ideas, had at their disposal very scanty material and yet recorded unusual forms.

Later I shall also show that the prognosis of sporadic acute poliomyelitis and that of epidemic acute poliomyelitis differ relatively less than was formerly alleged; and that the epidemic behavior is in no way distinctive, as was shown by my observations upon the Swedish epidemic, and presents all possible degrees from apparently isolated sporadic to accumulated and more or less pronounced epidemic cases. The map of the distribution of acute poliomyelitis in the Swedish outbreak shows that the disease occurred in foci, within each of which usually a continuity of spread could be demonstrated. Such was the case in those parts of the country in which the disease appeared not in epidemic form but only as isolated sporadic cases. From what I have said there can be little doubt that epidemic and sporadic poliomyelitis are one and the same disease.

*Etiology.*—Infantile paralysis has from earliest times been attributed to a variety of causes; *e. g.*, trauma, cold, teething, etc. Infectious diseases, such as scarlet fever, measles, and pneumonia, rarely were alleged to be the cause, and a belief arose that under certain circumstances their toxins could produce infantile paralysis.

In 1887, Strümpell—and later Pierre Marie—stated that infantile paralysis was a disease *per se,* independent of other infectious maladies. Experimental research and the study of epidemics have since adequately confirmed this statement. Naturally, a specific organism was early sought but as none was found either in cultures or in spinal cord sections, the morbid changes were attributed to the action of a toxin. During the last decade several microorganisms from the spinal fluid in this disease have been announced. Fr. Schultze, Concetti, Looft, Dethloff and others whose examinations were restricted to single cases, and Geirsvold and Potpeschnigg who investigated large series, all reported such

findings. Usually an organism resembling the Weichselbaum micrococcus was incriminated. Other investigators with similar material have however failed to obtain corroborative evidence of these discoveries. The efforts to demonstrate organisms in sections of affected tissues have likewise proved unsuccessful. Bonhoff by means of the Mann stain demonstrated in the glia cells, bodies which he alleges to be specific. The results of experimental investigation have shown that the bacteria found have absolutely nothing to do with Heine-Medin's disease, and that in those cases in which they arose not from faulty technique, such bacteria must be regarded as having had an accidental and not a causal relation to the malady.

*Experimental Poliomyelitis in Monkeys.*—Before discussing the recent successful inoculation experiments in monkeys, I shall first refer to earlier experimental researches upon acute poliomyelitis. Roger, Gilbert and Lion, Vincent, Enriquez, and Hallion; Thoinot and Masselin, Crocq fils; Ballet, Charrin, and Claude have produced poliomyelitis with various bacteria. But as I have already mentioned no one has succeeded in reproducing more than a vague semblance of the disease. I, myself, notwithstanding the extensive material employed, could obtain only negative results with streptococcal injections. The time has fully arrived when such experimental investigations should be discarded from the literature of this disease.

Landsteiner and Popper were the first experimentally to reproduce indisputable poliomyelitis. They took a piece of the spinal cord of a boy who had died of acute poliomyelitis and introduced it into the peritoneal cavity of a monkey. They were able to reproduce a disease characterized by paralysis and associated with the pathologic-anatomic changes of acute poliomyelitis. The results of Landsteiner and Popper were extended and corroborated by several observers. Similar investigations by Landsteiner and Präsek, Flexner and Lewis, Knöpfelmacher, Leiner and von Wiesner, Römer, Römer and Joseph, Levaditi and Landsteiner, and Netter and Levaditi were carried out about the same time practically independently of each other.

It should be mentioned, in passing, that similar experiments have been made with many other animals, but no constant results have been obtained. Thus, Flexner and Lewis—who have done

most work in this field—failed in numerous experiments to cause the disease by intracerebral inoculation of guinea pigs, rabbits, horses, calves, goats, pigs, sheep, rats, mice, dogs, and cats. Most observers have found animals other than monkeys to be refractory. But Krause and Meinecke, also Lentz and Huntemüller, have reported as many successful transmissions in rabbits by inoculation through the blood stream, as in monkeys by intraspinal inoculation. Insignificant pathologic-anatomic changes were found in the spinal cord of the rabbits. Meinecke explains most of the negative results of other experimenters on the grounds of variation in the susceptibility of different breeds of rabbits and of insufficiency in the amount of the infective material injected. These features are, however, negligible factors in monkeys in which a minimal dose suffices to produce the disease. It seems to me, with so many contradictory statements about poliomyelitis in rabbits, that until we have further information only monkeys should be used for clinical research purposes, for failure to reproduce the disease by inoculation is in them exceptional.

The clinical picture of monkey poliomyelitis corresponds very closely to that in man. The most important distinctions are the absence in monkeys of the initial fever, and the frequency with which the disease is characterized throughout its course in them by subnormal temperature. Prodromal symptoms sometimes usher in the paralysis but are often absent. The paralytic signs develop in rapid succession. The brunt of the attack falls upon the legs; and a flaccid paralysis develops which is characterized by atrophy and loss of reflexes. The mortality among monkeys is very high. In Flexner and Lewis' experiments the death rate among 81 monkeys was 54.3 per cent. According to these observers the incubation period, from the injection until the onset of paralysis, is 9–10 days; its minimum is 4, and its maximum 33 days.

The pathologic-anatomic picture—apart from the results of Leiner and von Wiesner—corresponds with that which we find in man. The most important results yielded by experimental investigation are, however, those which relate to etiology and pathogenesis. Examination of sections of human and of monkey's tissues and the study of the cerebrospinal fluid, blood, etc., by every conceivable method have given uniformly negative results.

These failures led many to the belief that poliomyelitis is a toxæmia. Experimental investigation has now proved the incorrectness of this belief. The virus occurs in the spinal cord. By injecting virulent material into the brain the spinal cord is made virulent and we can then reproduce the disease in monkeys by intracerebral inoculation with this virulent spinal cord tissue. The virus has thus been propagated through many generations of monkeys.

The virus shows a special affinity for the spinal cord. Wherever it be injected it will be found mainly localized in that organ. But it has not been demonstrated in the blood, spleen or any other organ of the monkey. Yet it seems to be eliminated by several channels, for after intracerebral injection it has been found in the salivary and mesenteric glands and in the nasal mucous membrane. In the spinal cord its potency is preserved for some time but soon diminishes and finally disappears; at least Levaditi and Landsteiner observed that the spinal cord about six weeks after infection was no longer virulent.

The interesting fact has, moreover, been established that the virus of acute poliomyelitis cannot be classed among the common bacteria, for it passes through bacterial filters such as the Berkfeld. When fluid containing ordinary bacteria is so filtered, the filtrate is sterile: in poliomyelitis the filtrate is infective; hence the virus belongs to that class which we usually designate filtrable. It closely resembles, in many of its characters, the virus of rabies. One property which both enjoy is resistance to the action of glycerin. This resistance distinguishes them from all ordinary bacteria. Römer and Joseph found the virus after almost five months in undiluted glycerin potently infective; but other observers have recorded an attenuation of the virulence under similar conditions.

The poliomyelitis virus is also markedly resistant to other agents. Flexner and Lewis, for example, found the infectivity still preserved after exposure for forty days to a temperature of from —2° to —4° Celsius; and, after fifty days, at —4° C. During the exposure autolysis appeared in the preserved pieces of the cord which were covered with mould, and yet the virus remained unimpaired. Even to drying, the virus is most resistant. The experiments of Leiner and von Wiesner show, however, that

if the virus be allowed to dry in thin layers of infected tissues, if it be allowed to desiccate therefore under conditions which approximate to actual experience, it rapidly decreases in virulence. The poison is more sensitive to high than to low temperatures. At 55° C. it loses its virulence, and at 45° C. it is perceptibly attenuated.

Much of the experimental research has been directed towards the question of acquired immunity and many interesting facts have been discovered. Flexner and Lewis, Landsteiner and Levaditi, and Römer and Joseph demonstrated that monkeys which recovered from one infection with the virus of poliomyelitis are immune. According to Joseph and Römer this immunity is present even when the first infection produces no clinical symptoms. Moreover, antibodies can be demonstrated in the blood of such immune monkeys. These antibodies can neutralize the action of the virus *in vitro* (Römer and Joseph, Landsteiner and Levaditi, Flexner and Lewis). Netter and Levaditi, and Flexner and Lewis have further shown that in the serum of children who have recovered from infantile paralysis, antibodies are present; and Netter and Levaditi have also established that these antibodies can be demonstrated in the abortive forms of the disease. Wollenstein, Römer and Joseph, and others failed, however, to demonstrate the presence of amboceptor (komplementbinden Antikorper) in the cerebrospinal fluid or in the blood serum of patients who were suffering from, or who had recovered from poliomyelitis. From similar investigations on monkeys they obtained negative results. Römer and Joseph call attention to the fact that if in highly immunized animals this absence of amboceptor is shown to occur, the analogy already recognized between poliomyelitis and rabies would be reinforced; for amboceptor has not as yet been demonstrated in rabies.

In has already been stated that no culture has been obtained from the spinal cord. Flexner and Lewis and Levaditi have, however, given us an impulse to the further study of the propagation of the virus outside the body for in bouillon prepared from the clear, bacterial-free, virulent spinal cord filtrate they have seen arise a cloudiness which was not due to any contaminating bacteria. With the aid of Borrel's modification of the Löffler method, Levaditi thought that he further observed in the cloudy bouillon

minute staining bodies of oval form. Römer and Joseph have found in examining these filtrates (Berkfeld) by means of the ultramicroscope, extremely small round oval bodies which were not demonstrable in the filtrates from normal spinal cords. Benecke, and Krause and Meinecke have also published similar results which they obtained in working with the blood of infected children. The results of experimental research in pathogenesis and other matters will be dealt with later.

*Predisposing Factors.*—From our experience of conditions in epidemics and from the results of experimental research, we are compelled to regard Heine-Medin's disease as a specific infection. A number of cases have been observed in which the disease has developed during the course of a common infectious malady. It is extremely probable that such cases are merely coincidences, and that the infectious malady is to be regarded in them only as an agent in the production of the favorable moment for the poliomyelitis invasion.

There is practically only one predisposing factor—the age. As is emphasized in the name, infantile paralysis, the disease usually attacks children. In order to show the incidence of the disease at different age periods, I shall quote some figures from various epidemics:—

| Observer | Epidemic | 0–3 Years | 3–6 Years | 6–9 Years | 9–12 Years | 12–15 Years | Over 15 Years | Summary |
|---|---|---|---|---|---|---|---|---|
| Medin | Stockholm, 1887, 1895 | 50 | 13 | 1 | ... | ... | 1 | 65 |
| Wickman | Stockholm, 1899 | 34 | 12 | 1 | 1 | ... | 5 | 53 |
| Wickman | Göteborg, 1903 | 11 | 5 | 2 | ... | ... | 2 | 20 |
| Wickman | Schweden, 1905 | 183 | 214 | 179 | 123 | 106 | 220 | 1,025 |
| Sammelbericht | New York, 1907 | 463 | 197 | 40 | ... | 21 | 8 | 729 |
| Emerson | Massachusetts, 1908 | 29 | 13 | 10 | 3 | 5 | 9 | 69 |
| Zappert | N.-Österreich, 1908 | 151 | 59 | 21 | 9 | 5 | 7 | 252 |
| Lindner u. Mally | O.-Österreich, 1908 | 37 | 19 | 15 | 13 | 7 | 5 | 96 |
| Fürntratt | Österreich, 1909 (Steiermark) | 125 | 135 | 85 | 41 | 43 | 43 | 450 |

Leegaard during the two epidemics he reported found the following figures:—

| | 0–4 Years | 5–9 Years | 10 14 Years | Over 15 Years | Total |
|---|---|---|---|---|---|
| 1899 | 12 | 5 | 7 | 30 | 54 |
| 1905 | 208 | 207 | 140 | 179 | 794 |

The experience of Ed. Müller in Hesse-Nassau was that not less than 96 per cent. of the total cases occurred within the first decade. Children over five years of age were relatively seldom affected: nine tenths of the cases occurred in those less than five years old. The disease incidence was markedly greatest in the latter half of the second year. Cases in the second or third decade were quite exceptional. Of seventy-six sporadic cases collected by Byrom Bramwell, forty-one occurred between 0 and 3 years; eighteen between 3 and 6; four between 6 and 9; one between 9 and 12; and four between 12 and 15; five were over 15; and in three the age was not ascertainable.

Heine-Medin's disease is therefore principally a disease of childhood. Celebrated writers have even stated that acute poliomyelitis does not occur in adults. But the statistics of Wickman and Leegaard, however, show that adults are by no means immune. Fr. Schultze, Rissler, Taylor, van Gehuchten, Wickman and others had already by pathologic anatomic examinations proved that the disease affects adults. Wickman saw a man of 46 years suffering from a typical attack, while his nine children living in the same house with him remained unaffected. It is possible that conditions change from epidemic to epidemic, so that the frequency of attacks upon adults varies. On the other hand, the great diversity of existing statements upon this point may partly be due to a lack of uniformity in the thoroughness of the reports.

Besides the age, no other predisposing factor is positively known to us. As regards sex, the cases during the various epidemics, of which I have data, occurred as follows:

| | Male | Female | Total |
|---|---|---|---|
| Medin (1887) | 22 | 22 | 44 |
| Medin (1895) | 15 | 6 | 21 |
| Leegaard (1899) | 31 | 23 | 54 |
| Wickman (1899) | 33 | 21 | 54 |
| Wickman (1903) | 8 | 10 | 18 |
| Wickman (1905) | 591 | 426 | 1,017 |
| Leegaard (1905) | 472 | 365 | 837 |
| Zappert (1908) | 130 | 97 | 227 |
| Lindner and Mally (1908) | 57 | 37 | 94 |
| Lovett (1907) | 131 | 103 | 234 |
| Lovett (1908) | 39 | 26 | 65 |
| Emerson (1908) | 42 | 27 | 69 |
| Ed. Müller (1909) | 53 | 47 | 100 |

These figures show that the male sex is somewhat oftener attacked than the female. But the source of this difference eludes us. Of Byrom Bramwell's cases, 43 per cent. were male; 56 per cent. female.

Déjerine has asserted that a neuropathic disposition is an important etiological factor in the development of acute poliomyelitis. Wickman, Medin and Leegaard, however, could not substantiate this assertion.

Even when I elicited proof of a neurotic tendency in a patient's family, I could not attribute any causal significance to it. Ed. Müller also calls attention to the fact that in his experience the children affected by acute poliomyelitis were free from neuropathic taint, and, as a rule, were physically and mentally normal. Johannessen, however, found various mental diseases among the families in several of his cases.

Occasionally, infantile paralysis has been reported in those whose relatives (uncle and aunt) had previously been affected (Wickman, Fürntratt). Leegaard attributes a certain importance to chills and reports strikingly numerous cases which followed exposure to cold and wet. Perhaps, however, we ought rather to consider such exposure as belonging to the general condition under which the people live. It is difficult to determine if over-exertion is a predisposing cause, but I am convinced that at least once the disease has begun, over-exertion has an unfavorable influence upon its further course.

Hochhaus and others have occasionally observed the disease to follow vaccination. This association is most probably accidental.

Finally, an acute atrophic paralysis may rarely arise from a variety of causes other than the virus which produces Heine-Medin's disease. A few cases are recorded of acute poliomyelitis probably due to syphilis; *e. g.*, J. Hoffmann's case. Some may be classed as cases of partial transverse myelitis. Typical Heine-Medin's disease has been observed to develop in a case of an existing luetic infection. Injury may cause a hematomyelia localized to the anterior horns, and thus simulating acute poliomyelitis (Beyer); but the history and onset serve readily to identify this condition.

## CHAPTER II

### Pathological Anatomy

To understand the various clinical forms of the disease, an exact knowledge of its pathological anatomy is indispensable. As research in recent years has enabled us definitely to ascertain the nature of the morbid changes, I shall in this chapter somewhat fully discuss them, particularly those peculiar to the acute stage.

*A. Acute Stage.*—As far as I know, the following are the observers who have published reports upon the acute stage.

| | |
|---|---|
| Rissler (1888) | 3 cases (5–8 days). |
| Dauber (1893) | 1 case (5 days). |
| Goldscheider (1893) | 1 case (12 days). |
| Siemerling (1894) | 1 case (8 days). |
| Redlich (1894) | 1 case (10 days). |
| Bickel and Roeder (1898) | 1 case (12 days). |
| Bülow-Hansen and Harbitz (1899) | 2 cases (resp. 5 and 7 days). |
| Matthes (1899) | 1 case (8 days). |
| Mönckeberg (1903) | 1 case (12 days). |
| Batten (1904) | 1 case (13 days). |
| Schmaus (1905) | 1 case (3 days). |
| Neurath (1905) | 1 case (2 days). |
| Wickman (1905 and 1910) | 14 cases (2–9 days). |
| Forssner and Sjövall (1907) | 2 cases (resp. 1 and 2 days). |
| Harbitz and Scheel (1907) | 13 cases (2 and 10 days). |
| Barnes and Miller (1907) | 13 case (8 days). |
| Cadwalader (1908) | 3 cases (3–6 days). |
| Marburg (1909) | 6 cases. |
| Hoffmann (1909) | 1 case (7 days). |
| Hochhaus (1909) | 2 cases (each 2 days). |
| Strauss (1910) | 8 cases (2–13 days). |
| Benecke (1910) | 3 cases. |
| Pirie (1910) | 1 case (5 days). |
| Marchand (1910) | 1 case. |

*Macroscopic Changes.*—As Heine-Medin's disease is an infectious malady, symptoms of a general infection are to be expected. Enlargement of the spleen has been present in some cases; and sometimes, cloudy swelling, even distinct inflammation, appears

in the kidneys. Rarely, subpericardial and subpleural hemorrhages have been observed, which may, in part at least, have arisen from terminal respiratory conditions. More often, a hyperplasia of the lymphoid tissue of the intestines occurs. Rissler was the first to describe the enlargement of Peyer's patches and of the solitary follicles. It is doubtful whether this lymphoid reaction is due to a local or to a general action of the virus. Beneke observed moderate enlargement of the tonsils with suppuration.

But the important and essential characteristics of the disease are the changes in the central nervous system.

The cerebrospinal fluid was found always clear and often increased. The only noteworthy change in the pia mater was hyperemia. No cellular exudate was ever noticed, in spite of the fact that microscopic investigation showed implication of the pia mater. Rissler reports two cases of hyperemia of the dura, also, with hemorrhages upon its external surface.

The changes in the spinal cord are usually obvious to the unaided experienced eye. If they are at all marked, the cut surface protrudes, the gray substance is hyperemic, either as a whole, when it appears as a red H, or only in circumscribed areas, especially in the anterior horns. Besides this diffuse coloring, generally, tiny blood specks and streaks also are perceptible; they resemble capillary hemorrhages and have been so reported. But in most of the cases they are actually only vessels distended with blood. As mentioned already, these macroscopical changes are most marked in the anterior horns, especially in the protuberances; but they occur also in the posterior horns and occasionally in the posterior horns alone (Mönckeberg). In the white matter usually edema and occasionally vascular distention are seen. The edema may be so great as to appear to the naked eye like a general softening of the cord. (Harbitz and Scheel report areas of softening of the spinal cord.) But on microscopical examination no "softening" in the ordinary acceptance of the term can be detected (Wickman). In certain cases, the cord seems practically normal to the unaided eye, but microscopic examination invariably reveals the presence of morbid changes (Rissler).

In fatal cases edema and hyperemia are found in sections at higher levels of the central nervous system. These changes may be so marked in the brain as to render the dura tense and the con-

volutions flat (Wickman). The pia may be hyperemic and very edematous (Daubert). The brain substance may also be hyperemic. The gray matter may occasionally show flecks of red (Redlich). Cerebral changes may be invisible to the naked eye, and microscopic alterations yet be present (Wickman).

The macroscopic changes in the transitional and end stages may be very slight. But if the destruction is extensive, the anterior horn appears shrunken at first and smaller than normal later, after a scar has formed. If only one side be affected, on cross section the cord is asymmetrical; the bundles of nerve fibers adjacent to the affected anterior horn appear smaller than normal and the roots arising from it are atrophied.

*Microscopic Changes.*—The pia mater. The pia is the seat of a round-celled infiltration. (Plate II, No. 1.) The majority of the round cells appear to be lymphocytes. But another kind of cells (Maximov's polyblast)—which I shall describe more fully in discussing the round cells of the spinal cord—also occurs in relatively great numbers. The Unna Marshalko plasma cells, large lymphocytes and fibroblasts are seldom seen. More frequent than these, though also rare, are typical polynuclear leucocytes with lobed nuclei and neutrophilic granules.

The spread of the infiltration in all of my cases showed considerable uniformity. The infiltration was especially marked in the lumbar and sacral regions of the cord, where it generally implicated the entire circumference. In the upper parts of the cord, it was less severe and could usually be seen only at the entrance of the anterior fissure, chiefly in the anterior fold of the pia. The infiltration was especially pronounced over the front of the cord. But in sections at higher levels, circumscribed areas of marked accumulations of cells also occurred in the pia. Forssner, Sjovall, and Marburg and Strauss observed further that the infiltration was particularly localized to the lower part of the medulla spinalis. In the cases reported by Harbitz and Scheel, the infiltration, although generalized, yet predominated in the lower parts and over the anterior aspect of the cord.

Some special peculiarities of the infiltration of the pia have yet to be mentioned. The contiguous bundles of medullated nerve fibers are rarely implicated. The infiltration of the pia is confined to the area around the vessels. At higher levels, where the

## PLATES I AND II

The representations of microscopical preparations are taken from my "Studies of Acute Poliomyelitis" and "Further Studies," etc.

PLATE I, No. 1. Round-cell infiltration of the ganglion cells of the lateral group of the gray matter, in the sacral region of the cord, from a case two and a half days after the onset.

PLATE I, No. 2. Ganglion cells from the same region in the same case, almost destroyed by phagocytic neuroglia cells (Neurophages).

PLATE I, No. 3. Infiltration of the lymphatic space of a central vessel from the lumbar cord of the same case.

PLATE I, No. 4. Infiltration of a vascular space and of the surrounding tissue in the anterior horn of the lumbar cord in the same case.

PLATE II, No. 1. Round-cell infiltration of the pia in the antero-lateral gray matter of the sacral cord, from a case of three to four days' duration.

PLATE II, No. 2. Area of round-cell accumulation in the posterior root entrance zone of the sacral region, in a seven-day case.

PLATE II, No. 3. Right anterior horn from the upper dorsal region of the same. Apex of the anterior horn is directed downwards. To the right and left of the section can be seen the much less infiltrated white matter.

PLATE II, No. 4. The greater part of the gray matter of the spinal cord in the upper lumbar region of the same case. Marked infiltration of Clark's column (to the right). The infiltrated anterior system with the entering central vessels below and to the left. Posterior columns below and to the right.

PLATE II, No. 5. Left anterior horn, apex downwards, from the dorsal region of the same case. The larger vessels chiefly infiltrated. Below, to left and right, can be seen the white matter, which is here very slightly affected.

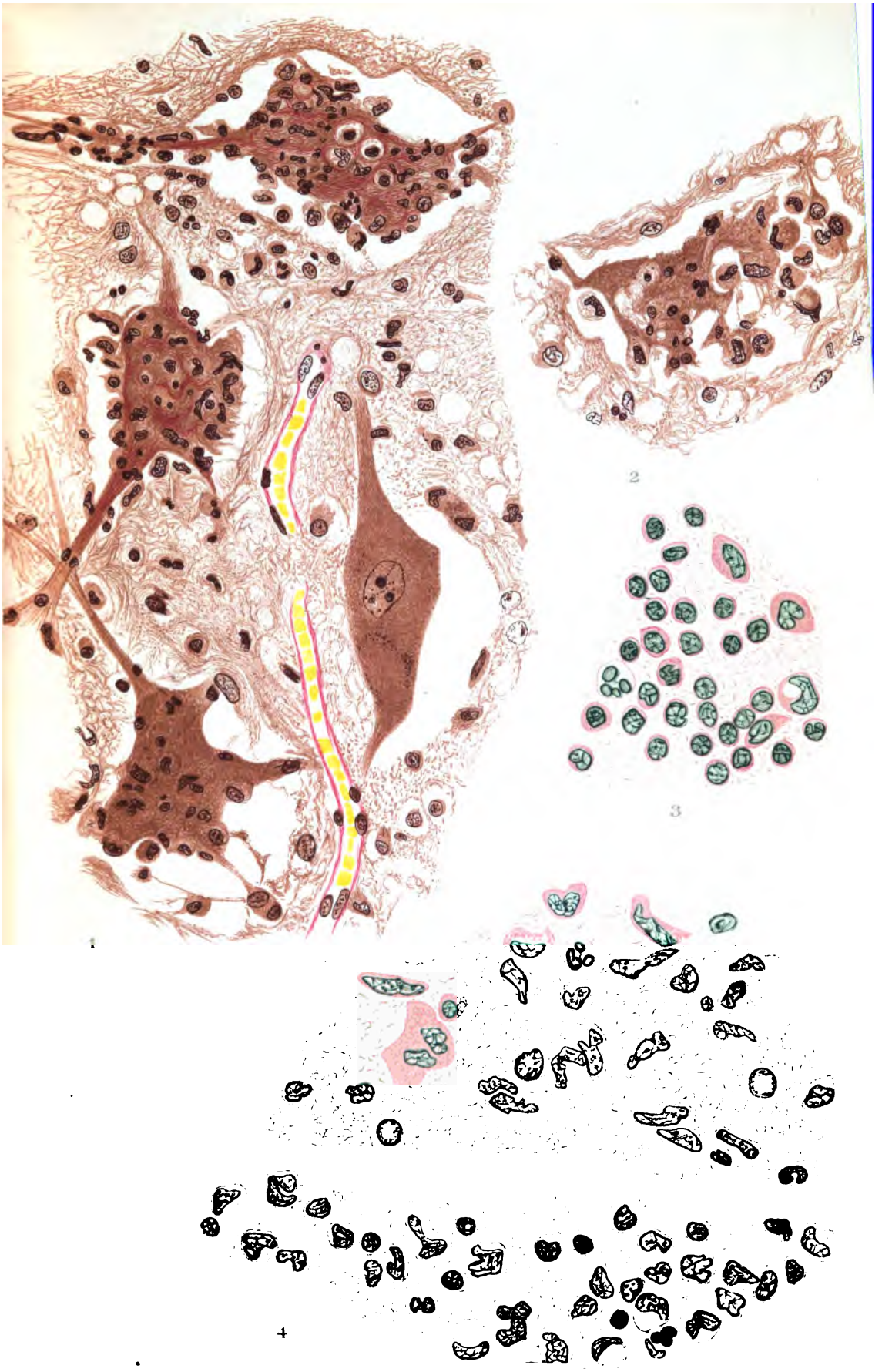
PLATE II, No. 6. Circumscribed area of disintegration from Clark's column in a two-day case.

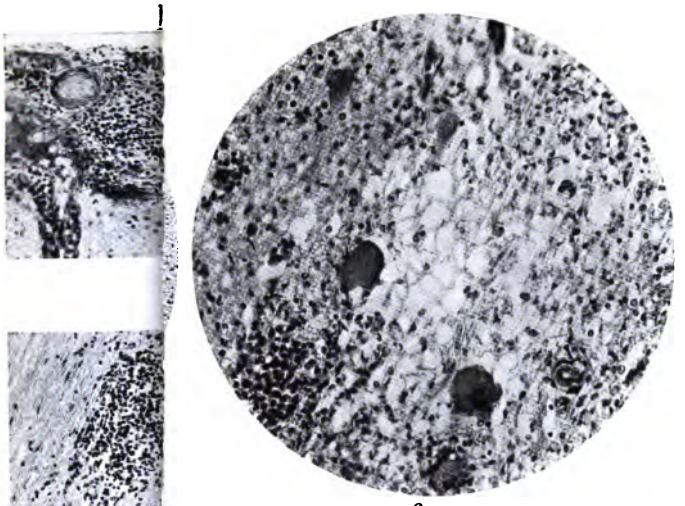
PLATE II, No. 7. Hypoglossal nucleus of the same case. Round-cell infiltration of the vessels and of the supporting tissue with normal ganglion cells.

PLATE II, No. 8. Area of round cells in the brain cortex from a seven-day case.

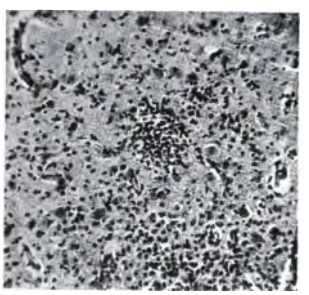
PLATE II, No. 9. Anterior part of the anterior horn, in the cervical enlargement, from a three weeks' case. The supporting and nerve tissue has been destroyed and absorbed. Only the vessels surrounded by multinuclear cells still remain.

PLATE II, No. 10. Anterior horn, apex downwards, of lumbar enlargement, from an eight weeks' case. The whole lateral half (left of plate) of the anterior horn is destroyed.





*6*



*8*



*10*

pia in the lateral and posterior parts of the cord is free from round cells, the infiltration around the vessels stops at the periphery of the spinal cord and does not involve the pia. It is noteworthy that in the dorsal and cervical regions, where the implication of the pia on the external aspect of the cord generally is either very slight or completely absent, the infiltration of the pia is still most obvious towards the bottom of the anterior fissure. Considerable infiltration may occur here and around the entrance of the central vessels, although the pia elsewhere escape. These facts are of importance, for they enable us to realize the relation of the changes in the pia to those in the spinal cord.

On microscopical examination, the pia is seen to be infiltrated, and its blood vessels are found to be dilated and congested. Inflammatory changes have been observed in the pia mater of the brain, also. The implication of the pia mater in infantile paralysis was noted first by Dauber, and subsequently by Bickel (Roeder and Schultze). Wickman established, and Harbitz and Scheel and others have since corroborated, that changes in the pia are a constant phenomenon of this disease.

The affection of the pia mater is of special interest, as it explains the meningeal symptoms, which, in the initial stages of otherwise typical spinal infantile paralysis, are sometimes observed. The affection of the pia is also the basis of the meningeal form of Heine-Medin's disease.

As a rule, the dura is not implicated. Harbitz and Scheel succeeded in demonstrating a slight cell infiltration of the dura mater in only two cases.

*Spinal Cord.*—The changes in the spinal cord are most evident in the interstitial tissue and in the vessels. Of these changes Rissler has written a classical description. The vessels are dilated and congested. The vascular changes are especially marked in the veins but are not confined to the larger vessels if the process is at all advanced. The capillaries are often greatly distended and tortuous. Siemerling and Matthes allege that a formation of new capillaries occurs. The contents of the vessels are red blood corpuscles.

Wickman, Harbitz and Scheel, and Strauss, in spite of most careful search, failed in all their numerous cases to find any evidence of thrombosis, or embolism, in the first stage of the disease;

and, as far as I know, all other investigators have similarly failed. Mott and Batten have each reported thrombosis in a single case. These cases, however, were respectively of 17 and 13 days' duration, and I believe it was a secondary phenomenon. Tiny hemorrhages in conjunction with the hyperemia occur not only in severely affected areas, but also in areas which otherwise show but little change. These hemorrhages are partly attributable to the inflammatory process. They may, however, partly be agonal changes, dependent upon the terminal respiratory paralysis. Siemerling's case showed, both in the lumbar and cervical regions, an extensive hemorrhage, which implicated the greater part of the anterior horn.

Hemorrhages are occasionally seen in the anterior horn, which explain the quite apoplectic type of paralysis sometimes observed. Motor disturbances may, however, develop with extreme rapidity solely from the inflammatory process.

More important than the hyperemia and hemorrhage is undoubtedly the cellular exudate. The cells are derived partly from the vessels and partly from the tissues. The first is the more constant source and in some sections the cellular exudate from the vessels is the only, or, at least, the principal pathologic change. (Plate II, No. 5.) The round cells which compose the exudate (in Fig. 11, No. 5) are situated in the adventitial lymph spaces of the vessel wall.

The infiltration of the adventitia is most marked around the entrance of the central vessels into the spinal cord at the bottom of the anterior fissure, where it is directly continuous with the infiltration of the pia.

It has been stated that the arteria centralis is the most severely implicated. But Wickman maintains that in his cases, so far as any difference in severity existed, the veins were more gravely affected than the arteries. Between the central and the peripheral vascular systems, with the exception of the severity with which the larger central vessels tend to be affected soon after entering the spinal cord, no evidence of any discrimination exists. Harbitz and Scheel, and Strauss also state that the veins are the more affected. Marburg, on the contrary, in his recent report of his cases, states that even at the very onset of the disease, the anterior horn shows dense infiltration around the arteria centralis. In rare

instances, quite independent of other changes, relatively slight infiltrations occur around the peripheral vessels, especially the veins. Besides this infiltration of the adventitia, a perivascular exudate is sometimes seen. The round cells penetrate the surrounding tissues and enclose the vessels like a wall.

In the supporting tissue itself, masses of round cells often collect. These cells are derived from the vessels. Thus, in Plate II, No. 1, the upper left hand portion of the picture (anterior horn) shows the exudate to consist principally of perivascular cell groups surrounding the minute blood vessels and capillaries, around whose branches they are massed like clusters of grapes on the stem of a vine. When an area of dense cellular infiltration is present (Plate II, No. 3), its extent can be demonstrated by serial sections, to be limited to the area of distribution of a blood vessel. In other cases, the infiltration, however, is diffused through the supporting tissue and is without any apparent relation to the vascular supply. In some areas, an unmistakable relation to the ganglion cells can be observed. Forssner and Sjöval demonstrated that many of the small masses of cells are only the remains of neurophages, which have completely devoured the ganglion cells.

The morbid changes we have been dealing with occur chiefly in the anterior horn. But in the posterior horn, analogous alterations are almost constantly present. In most of my cases such changes were especially marked in Clarke's column in the lower dorsal and upper lumbar regions. (Plate II, No. 4, right.) Occasionally I was able to prove that the infiltrations were connected with the vessels of the posterior system. But recently I have sometimes found Clarke's column scarcely affected. In Marburg's experience, Clarke's column was invariably less affected than the anterior horn. As a rule, the changes in the posterior are less marked than in the anterior horns. But this rule has exceptions. For instance, the morbid process may extend with the same severity throughout the greater part of the gray matter; or it may, as in the lower dorsal region in the majority of my cases, affect mainly the boundary zone between the anterior and posterior horns and gradually diminish in intensity towards the front and the back of the cord. Rarely the posterior horn is affected to a greater degree than the anterior. Cellular infiltration may occur in the

white matter, as well as in the anterior, posterior and lateral horns; it is most constantly observed in relation to the sheaths of the blood vessels but, as Redlich first recorded, it may be seen also in small groups within the nerve tissue. I, myself, demonstrated in almost all of my early cases minute and rare foci of cell infiltration among the white nerve fibers. (Plate II, No. 2.) Such a small focus is pictured in the entrance zone of the posterior root. Diversity of opinion still prevails concerning the nature and origin of these round cells. While Rissler, Redlich, Schmaus, Harbitz, Scheel and others described them as migrated leucocytes, Goldscheider, recently joined by Strauss, maintains they are proliferated fixed tissue elements. The former have focused their attention principally upon the glia cells; the latter, upon the cells of the adventitia. According to Marburg, all are lymphocytes.

In my latest study of the pathologic anatomy of this disease, I think I have solved the problem of the nature of these cells. The principal cells are not leucocytes, nor proliferated connective tissue elements, nor are they simply lymphocytes. They represent a further stage in the development of the lymphocyte and are what Maximov has described as polyblasts. The distinguishing features of these cells are shown distinctly in the preceding plates. Plate I, Fig. 3, represents the exudate around the wall of a large-sized vessel. To the left can be seen only one cell, whose protoplasm remains unstained (stain, Pappenheim's methyl, green and pyronin); four are obviously polynuclear leucocytes. The remaining round cells can be divided into two groups, one of typical lymphocytes, encircled by a small amount of pink staining protoplasm and containing a dark staining nucleus, rich in chromatin, which is aggregated at points into masses, the other of cell elements which evidently are derived from lymphocytes, in which the nucleus stains lightly, in which a dainty network distinctly appears, and in which the protoplasm has increased. These cells later develop into types—as is evident from three or four of the larger forms in this figure—which have no resemblance to the mother cells, to which, however, numerous intermediate forms link them. The origin of these cells from lymphocytes may therefore be considered as proved.

Let us now pass to the infiltration around the small vessels and

in the supporting tissue. The same cell elements occur but they are now characterized mainly by the increase in the amount of their protoplasm (Plate I, Fig. 4). This figure consists of two parts, which are separated by a diagonal light zone due to shrinking of the preparation. The upper part shows a tissue infiltration; the lower, in which the round cells are denser, shows an exudate around a small branch of the same central vessel, from which the infiltration of the lymphatic space depicted in Fig. 3 was obtained. These infiltrations are continuous and arise from the same infiltration. The same cells as have already been mentioned, lymphocytes, leucocytes and polyblasts, are present in this figure. The polyblasts now consist of immense cell masses, possessing a light staining reticulated nucleus and abundant protoplasm; they are here in greater number and show a still higher development than before. In the tissue infiltration, two isolated glial nuclei and one leucocyte can be observed, but no typical lymphocytes. Lymphocytes can, however, be seen in the adjoining vascular infiltration.

Obviously, the relative numbers of lymphocytes, leucocytes and polyblasts are not everywhere the same as is here depicted. In some places the lymphocytes are in the majority; in others, the leucocytes. As a rule, however, in the tissue infiltration, the mass of the round cells consists of polyblasts. Pirie and I arrived at this conclusion almost simultaneously.

Another interstitial change which plays an important part in the appearance and disappearance of the symptoms has yet to be considered, namely edema. To the naked eye, in many cases, edema is obvious. Indeed it is generally easier to detect macroscopically than microscopically. It is at least partly responsible for the appearance, which the glial tissue often presents, of being permeated by or converted into a finely granular substance. Sometimes the tissue seems to be loosened, so that the glial meshwork appears wider. In a few of Wickman's cases, circumscribed foci of softening were present in Clarke's column. In the lighter parts of Plate II, Fig. 6, only the remains of the delicate glial reticulum can be perceived. Bülow-Hansen, Harbitz, Forssner, Sjövall and others also describe a sponginess of the tissues. I think the edema is of no slight importance from a clinical point of view, as it affords a plausible explanation for the rapid disappearance of a paralysis. The dread change which gives rise to the paralysis has its seat in

the ganglion cells of the anterior horn. Strauss, by means of Bielschowsky's method, has recently shown atrophy to be the initial change in the intracellular network of the neurofibrillæ. By the use of Nissl, Von Gieson and other methods of staining, the cell body has been proved to swell and to become more globular. With this swelling a disintegration of the Nissl granules occurs and often extends throughout the whole cell. If a section of such a swollen cell does not implicate the nucleus, the entire cell appears to be changed into a homogeneous anuclear structure, frequently without a single process. But serial sections usually demonstrate that this appearance is deceptive, for the nucleus and the cell processes can be found in contiguous sections. In many cases, the nucleus retains its normal appearance for a remarkably long time. Generally, it also conserves its normal position in the middle of the cell. When a severer change occurs in the cell body the nucleus is converted into a deeply staining, irregularly shaped structure. Sometimes complete karyolysis happens. Occasionally vacuoles in varying number are studied through the protoplasm.

The severity of the ganglion cell changes usually is in direct ratio to the intensity with which the interstitial tissue is affected. No nerve cells, as a rule, are visible, in the largest infiltrations, but slightly altered ganglion cells are sometimes present in the midst of a markedly infiltrated area. On the other hand, degenerated cells unaccompanied by interstitial changes have never yet been found in man. The interstitial changes do not necessarily consist of pronounced cell accumulation; edema may prevail. Degeneration of the ganglion cells without inflammatory reaction occurred in a case of Cestano-Savini and Savini, but this particular case clinically as well as pathologically differed so widely from all others hitherto described, that I fully agree with Strauss that it was not a case of acute poliomyelitis.

Remarkably numerous neurophages were described by Forssner and Sjövall, who attributed to them considerable importance in the degeneration of nerve cells. In my later cases I have fully confirmed these observations. As shown in Plate I, Figs. 1–2, round cells invade and ingest the ganglion cells till only a clump of round cells with greatly increased protoplasm remains to mark the site of the ganglion cell. In this process the polynuclear leucocytes and the polyblasts are the chief, if not the sole, agents.

According to Wickman, each acts quite differently. The polyblasts alone are active neurophages. In the middle of many ganglion cells, degenerating polynuclears lie; but around the periphery the polyblasts are situated and generally show no retrogressive changes. The difference in behavior of the polynuclear leucocytes and of the polyblasts is especially noticeable in places where the ganglion cells have already been ingested. In Fig. 1, the two polynuclear leucocytes, which are somewhat to the left above and to the right below the center of the field, remain quite passive; whereas, the protoplasm of the polyblasts is swollen and laden with tiny particles of fat. In addition, other ingested material, appar-

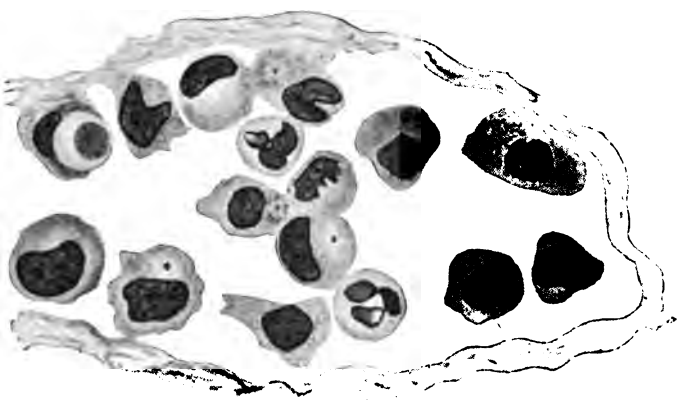


FIG. 1. Neuronophages, in which the difference in importance between polynuclear leucocytes and polyblasts is plainly shown.

ently decaying ganglion cells, is present. These fat-laden polyblasts develop later into typical fat cells.

The neurophages also occur in poliomyelitis in monkeys (Landsteiner and Levaditi, Landsteiner and Präsek) and are, I think, a feature especially peculiar to the most acute cases. In cases of slower course, the changes earlier described are evident. In perhaps not a few, a degeneration which I described in my first work on this subject, occurs; the peripheral part of the cell body degenerates and dissolves, but the nucleus is spared. If such cells are situated in areas of infiltration, the appearance may resemble a complete absorption of the ganglion cells, unless a careful examination with a high power lens be made, when the presence of the

ganglion cells will be detected. Strauss has since confirmed these observations.

In general, the nerve filaments of the gray matter are faintly stained and of irregular contour. Sometimes they show little swollen nodes like a chain of pearls; usually they are degenerated; sometimes only fragments can be recognized.

The parenchymatous changes in the posterior are analogous to, but not so marked as, those in the anterior horn. The difference lies in the slighter interstitial changes and the lesser implication of the nerve cells in the posterior horn.

In the region of the central canal, Wickman observed round cells, which in places penetrated between the ependyma cells; but the evidence of inflammation in this neighborhood was scanty.

In the bundles of white nerve fibers round cell accumulations are few and contain no nerve filaments. The changes in the white matter are very slight, and are due chiefly to edema. Swelling of individual axis cylinders has been noted; but with Weigert's method, at least in my cases, only imperfect staining was demonstrable. Rissler observed degeneration and tortuosity of the axis cylinder. In the acute stage, the changes in the posterior and anterior roots are very mild: they consist chiefly of the invasion of the fasciculi of the anterior root by the pial exudate penetrating between the nerve fibers. The vessels of the roots may also be infiltrated. Enlarged axis cylinders in the anterior and posterior horns have been observed. Siemerling found that the Marchi stain produced an appearance of black dots in the extramedullary portion of the anterior and posterior roots. Redlich and Mönckeberg described degenerative changes in the peripheral nerves. As these changes were slight, and as no evidence of local inflammation was observed, the degeneration must be considered as secondary. This secondary degeneration is not often present.

Forssner and Sjövall were the first to examine the cells of the intervertebral ganglia. They were able to prove inflammatory changes. Their observations were later confirmed by Marburg and Strauss, but Harbitz and Scheel found the ganglion cells normal.

Microscopic examination of the spinal cord has not yet revealed bacteria. Bonhoff, however, has demonstrated, by Mann's method, nuclear enclosures in the neuroglia cells, which he believes to be foreign bodies of a specific nature.

*C. Medulla Oblongata and Pons.*—Changes in the medulla oblongata have hitherto been found in every fatal case of Heine-Medin's disease in which they have been sought and in which death was not due to an intercurrent malady. The nature of the lesions here, as was first shown by Rissler, is identical with that found in the spinal cord. Wickman, however, has pointed out that the findings in the spinal cord differ regularly from the findings in the bulb; that in the bulb, the degenerative are less marked than the infiltrative changes; the lesions tend to be disseminated; and no preponderating localization in the motor areas—such as is seen in the spinal cord—occurs. The most intense changes in the bulb appear often apart from the nerve nuclei, in the substantia reticularis tegmenti. Exudates are visible in the most diverse areas; *e. g.*, in the cranial nerve nuclei of the olive; in the nuclei of the columns of Goll and Burdach; in the nucleus pyramidalis; in the substantia nigra; in the central gray matter in the neighborhood of the aqueduct of Sylvius; in the anterior and posterior corpora quadrigemina; in the raphe; and elsewhere. Forssner and Sjovall, Harbitz and Scheel, Strauss, J. Hoffmann, and others subsequently corroborated these observations.

In the gray matter, morbid changes are conspicuous in the larger vessels running beneath the floor of the ventricle. The tissue infiltration has an inconstant relation to the nerve nuclei. Sometimes the round cells congregate about the nuclei; sometimes they are grouped in the vicinity of and only slightly encroach upon the nuclei; and sometimes they leave the nuclei wholly untouched. Occasionally, a densely infiltrated vessel may be seen wandering through an otherwise intact nucleus; or almost the whole cross section of a nucleus may be normal and free from infiltrating cells except in one part where an exudate accompanies a vessel.

In general, the alterations of the ganglion cells are slight and are mainly chromatolytic. Where interstitial changes are absent the ganglion cells always appear normal, even when stained by toluidin blue. This may often be observed in the immediate neighborhood of infiltrated vessels, and, also, in places where infiltrations are not intense (Plate II, Fig. 7). Usually the more evident the infiltration the more do the ganglion cells suffer. But it is remarkable how exceptionally well preserved the ganglion cells

may be in the midst of a densely infiltrated zone (Wickman, Forssner and Sjovall, Harbitz and Scheel, Strauss).

An exact knowledge of these relations of the interstitial to the nerve cell changes is of great importance as regards pathogenesis.

*D. Brain.*—Redlich was the first to demonstrate that exudate around the vessel walls and small foci of round cells—evidences of inflammatory reaction—occur also in the brain. In all hitherto examined cases these brain lesions have been minute. Harbitz and Scheel made the most thorough investigations of the nature and site of the cerebral lesions in acute poliomyelitis. They found the basal part of the brain, particularly the neighborhood of the Sylvian fossa and the central ganglia, as a rule, to be more intensely inflamed than the surface convolutions; and that the central was the gyrus most often implicated. They further noted the involvement of the cerebral meninges, especially in the region of the Sylvian fossa. I shall later refer to two cases of encephalitis reported by them.

In five cases, in which Wickman had an opportunity thoroughly to examine the brain, much milder changes were present, especially in the pia. But even in these cases, scattered small foci, mostly in the central ganglia and in the central gyri, were observed (Plate II, Fig. 8).

The cerebellum presents analogous pathologic changes.

*E. Other Organs.*—The internal organs have seldom been investigated. Parenchymatous degeneration of the heart, liver and kidney—occasionally even a distinct nephritis—has been reported. Inflammatory changes outside the nervous system have been observed in the pericardium only, and in but a single case (Wickman).

*Reparative and Cicatrizing Stage.*—I shall describe this stage very briefly as from every point of view it is of much less interest than the acute stage. I have already related how, even at the height of the small celled infiltration granule-containing cells, which develop from the polyblasts, appear between the small round cells. Absorption thus commences. After a while, if the process were diffuse and severe, one can no longer speak of the tissue proper; the tissue is dissolved, melted and ingested by these granular cells (Plate II, Fig. 9), which lie partly scattered, but mainly concentrated around the lymphatics of the vessels. The support-

ing tissue and the neural reticulum are replaced by a granular substance, which is intersected, as by coarse threads, by processes of newly formed glial cells. Not even débris of the nerve elements may be detectable in these severely affected areas (Plate II, Fig. 10).

The small cell elements do not behave in this as in the acute stage. Besides the granular, typical Unna-Marschalko plasma, and distinctly proliferating glia, cells are present in great numbers. Spindles and other derivatives of the adventitial cells occur. Later, the granular cells gradually retreat till they are chiefly restricted to the lymph sheath of the vessels, where they may occasionally remain, even as long as two years after the onset of the disease (Roger and Damaschino, Lövegren). The neuroglia becomes more distinct and its cells develop so many wide and much branched processes that they resemble seaweed-covered stones. These processes gather together and the neuroglia loses its normal delicate felt-like appearance. The change advances. Naturally, the appearances observed in cicatrization depend upon the extent and severity of the destruction in the acute stage. If the entire anterior horn were then implicated to a degree which resulted in complete destruction, it would now appear atrophied even to the naked eye; and on microscopic examination, only neuroglia would be seen. In some cases such definite gliosis is present only in limited foci and normal areas still persist in the anterior horn. But if the destruction during the acute stage were not so intense, a more or less marked thickening of the neuroglia with rarefaction and atrophy of the nerve elements ensues. Obviously all possible degrees of transition between these various conditions may occur.

The changes in the ganglion cells originally reported by Prévost and Vulpian were later confirmed by Lockhart, Clarke, Charcot, Joffroy and subsequent investigators. It was observed in some cases that ganglion cells were affected in groups (Sahli, Déjerine and Huet). But within the affected groups, isolated normal ganglion cells still persisted in varying number at different levels of the cord. In one case Lövegren noticed that the boundary of an inflammatory focus ran across a ganglion cell group. Kawka, Goldscheider and Kohnstamm were able to demonstrate that the sclerosed areas are associated with thickened vessels. Groups of

round-cell infiltration have also been found in the posterior horn and in Clarke's column (Parrot, Joffroy, Déjerine, Huet, v. Kahlden and Praetorius).

The sequelæ of the initial destruction in the anterior horn are most evident: they consist of degeneration and atrophy of the intraspinal tracts, of the anterior roots of the motor nerves, and of the muscles.

Jagic, Bing and Mott have demonstrated by the Marchi method secondary degeneration in the antero-lateral and cerebellar tracts and in the posterior columns. The same changes can be seen in the anterior roots. The degeneration is followed by atrophy, which is usually well marked in the region of the antero-lateral tracts (Cornil).

The muscles, also, atrophy. Occasional hypertrophied fibers occur between the atrophied (Déjerine, Lövegren). Sometimes the muscle fat is increased.

Bing and Jagic were able to demonstrate in the pons, during the transition stage, morbid changes of slight extent. Eisenlohr observed in a doubtful case of several years' duration, a patch of sclerosis with degeneration of the ganglion cells in the facial nucleus.

Similar changes have been noticed in the brain: Lamy found, in addition to the usual changes in the spinal cord, four small sclerotic foci in the cortex of the left hemisphere, one in the parietal, the others in the frontal lobe. In Rossi's case, the remains of the encephalitic process were much more diffuse; part of the frontal lobe, the inner surface of the paracentral lobule on both sides, and the greater part of the corpus callosum were implicated.

In the cases reported by Sander, Rumpf, Colella and Probst, a flaccid paralysis of the extremities was associated with atrophy of the central convolutions. This cerebral atrophy was explained as secondary to the destruction of the peripheral neurons.

## CHAPTER III

### Pathogenesis

Charcot and Joffroy, who were among the first to investigate the pathology of the disease, taught that acute poliomyelitis was a parenchymatous process; that the ganglion cells attacked by the virus were destroyed; and that an inflammatory reaction followed. This teaching was based upon observation of a case in which several years after the initial attack the principal lesion discovered was destruction of the ganglion cells. This conception of acute poliomyelitis as a systemic disease corresponds completely with the clinical picture. In Charcot's day, as only cases of long standing were examined, the opinion prevailed that the disease produced a purely motor paralysis. Hence, little attention was paid to the observations of Roger and Damaschino, who laid special stress upon the interstitial nature of the changes, but who left open the question why the changes were limited to the anterior horns.

Rissler and v. Kahlden strongly advocated Charcot's theory. Rissler supported his advocacy by citing one special case in which the infiltration of the vessel and of the interstitial tissue was less marked than the degeneration of the ganglion cells. I should like to emphasize that he was the first to record and depict these interstitial changes. Further, he did not blindly adhere to Charcot's tenets, but admitted the possibility that the disease virus might simultaneously implicate the ganglion cells and the vessel walls. As von Kahlden relied solely upon observation of chronic cases, his horizon was limited.

All recent observers agree that Charcot's doctrine is untenable. The changes beyond the motor region, for example, in the posterior columns and in the pia, are not explicable as secondary to degeneration of ganglion cells; nor is there, at least in many areas, a primary affection of the ganglion cells. Thus, in the bulb, in distinctly infiltrated areas, even with our modern delicate staining methods, the ganglion cells appear normal. At first sight, such a condition as is depicted in Plate I, Fig. 1, where neurophages occur in the midst of a densely infiltrated tissue, seems to support Char-

cot's theory. But if the figure be more closely examined, even here, all the larger vessels are seen to be infiltrated, and the process must be regarded as inflammatory. Its inflammatory nature becomes still less open to doubt if, in such a case, different parts of the central nervous system be examined. Indeed, inflammatory changes only in the vessels and in the interstitial tissue may occur. But the importance of the activity of the neurophages must not be overlooked. As I have said, their activity, especially in the most acute cases, undoubtedly plays an essential part in the degeneration of the ganglion cells; but pathologic examinations have already shown that even in individual cases this is by no means true for all parts of the central nervous system. Nor is it tenable in those cases in which extensive and well marked paralysis disappears completely in a very short time, for a neurophagocytic action of considerable degree is quite incompatible with speedy return of function.

There is reason to expect that experimental investigation will throw some light upon this question. Unfortunately, at present, we have extensive microscopic observations only of poliomyelitis in monkeys. Leiner and v. Wiesner have reported some cases of degenerative processes in the ganglion cells unaccompanied by inflammatory reaction. We must here admit that there is a strong direct action of the virus upon the ganglion cells. It is also certain, however, that no parenchymatous process can adequately explain the known changes in man. The descriptions of Landsteiner and Popper prove, moreover, that a purely parenchymatous affection rarely occurs even in monkeys. Leiner and v. Wiesner acknowledge that in a large number of cases infiltrations exist; they suppose that the parenchymatous and interstitial processes develop synchronously; and they maintain in their writings a position intermediate between the extremists of both parties. I may here remark that the apostles of the inflammatory nature of the malady do not attempt to deny the direct action upon the ganglion cells. As I belong to this category, allow me to quote from my latest work on the pathology of this disease. Emphasizing the fact that, in man, many factors undoubtedly point to the interstitial, as the more important changes, I call attention to the undeniable possibility of a direct influence upon the nerve tissue. It is possible that under certain conditions this influence may even

be very marked, although, as a rule, it is slight. Among such conditions, extreme virulence of the infection ranks first.

It would not be surprising if an increase of virulence influenced the toxic peculiarities of the virus. Such a circumstance, however, can hardly affect our conception of the nature of the changes. Probably passage from monkey to monkey enhances the virulence.

Most recent investigators believe the changes in acute poliomyelitis to be inflammatory. Goldscheider, Redlich, Bülow-Hansen and Harbitz, Wickman, Harbitz and Scheel, Benecke, and others regard the degeneration of the ganglion cells as a special consequence of the interstitial inflammation. Ernst, Schwalbe, and others consider the parenchymatous and interstitial changes as synchronous. Many pathologists, however, believe that here, as elsewhere, it is immaterial whether an inflammation is discernible first in the parenchyma or not. The essential points to be determined in either case are the same: First, why the malady, which from a pathological standpoint is a strictly localized affection, develops clinically as a systemic disease; and, second, why the effects are limited practically to the anterior horn, and are not distributed as in a transverse myelitis.

Pierre Marie thought that Kady's experiments upon vascular distribution in the spinal cord solved the whole problem. Kady proved that the anterior horns are supplied from the central artery which, at the bottom of the anterior fissure, enters the spinal cord and turns forward to ramify within a restricted zone. Pierre Marie supposed the morbid process to consist of embolism or of thrombosis of the central artery. His theory received some support from the experiments of Hoche and Marinesco. It was generally accepted. I, however, felt compelled to raise the following objection to it:

1. In recent cases, neither embolic nor thrombotic processes have been demonstrated. Mott, Money and Batten have, it is true, each reported a case where thrombosis was present. But the most recent of these cases had already lasted thirteen days and such thrombosis may better be interpreted as a secondary process. In more recent cases, in spite of eager searching, thrombosis has not been found. And the isolated observations just reported are totally inadequate to permit a generalization.

2. The changes in Heine-Medin's disease are radically different

from those of an embolic process. The necrotic area which is characteristic of embolism is never observed in poliomyelitis.

3. Experimental embolism in the spinal cord does not substantiate Marie's hypothesis. Occasionally lesions restricted to the gray matter have been produced; whereas, usually the white matter is extensively implicated.

4. In ulcerative endocarditis, caisson disease, and other maladies in which demonstrable embolic processes do occur in the spinal cord, no preferential selection of the gray matter can be seen.

Proof has not yet been given that the changes in Heine-Medin's disease are referable to embolic or thrombotic processes; and, further, the pathology of the spinal cord comprises no analogous conditions to lend support to this view.

I have also emphasized facts—apart from the nature of the process—which seem to me to contraindicate any preponderating influence of the central artery:

1. In recent cases the most marked changes usually appear within, but never coincide with, the area of distribution of the central artery. Beyond this particular vascular zone, in the posterior horns, in the white matter, and in the pia, round-cell infiltration generally occurs. Clearly, since the central artery sends no branches either to the posterior horns or to the pia, the central artery cannot be implicated in lesions in these situations. Lesions of the white matter have been alleged to be distributed exactly within the area of supply of the central artery, but I believe otherwise. Kady's experiments show that in a transverse section of the spinal cord, three vascular zones can be distinguished: a peripheral zone, which is supplied exclusively by the peripheral artery; a central, limited to the gray matter, supplied by the central artery; and an intermediate, which is supplied from each side in such a way that the capillaries of both systems intermingle. If the central artery determined the local distribution of the disease, one would expect that the lesions would radiate from the gray, far into the white, matter; and that they would appear wedge-shaped on cross section. Such lesions, however, have never been observed. The morbid changes commonly cease precisely at the line of demarcation between the gray and white matter; and when, as occasionally happens, the disease encroaches further, it extends

by the direct implication of the contiguous tissue, and not by propagation along the branches of the central artery.

2. Occasionally I found the round cells accumulated about the peripheral veins and associated in occurrence and distribution with the peripheral vessels. Around a fork-shaped peripheral vein, which is ramifying in the lateral part of the anterior horn, such an infiltration appears in Plate II, Fig. 3. This section seems to me to demonstrate distinctly how easily a false conception may arise. The focus here is wholly confined within the anterior horn. It is therefore within the extent of the region supplied by the central artery. But serial sections showed that the infiltration was associated only with this peripheral vein and not with the central artery.

3. I found, as a rule, infiltrations occurred in connection with the distribution of the largest vessels (or of the lymphatics).

I assert not that the central artery plays no part, but that it plays not the most important part, in the pathogenesis. The round cell accumulations are sometimes associated with it; but they are also associated with the central vein, and sometimes with the peripheral vessels. I believe that these cells are directly derived not from the blood vessels, but from the lymphatics of the blood vessels. In my earliest publication on this subject, I maintained that the specific pathologic changes could best be explained as a lymphatic infection. If we regard the disease as a blood infection, it is undoubtedly difficult to account for the continuity of the changes in the long axis of the cord in fatal cases; for in a vascular condition one would expect the scattered foci of invasion to be separated by normal areas. The continuity of the lesions and the tendency of the paralysis to spread from below upward seem to me to indicate a diffusion of the virus within the spinal cord and its membranes. And this diffusion obviously follows not the blood but the lymph channels—the lymph vessels and the lymph spaces. In corroboration of this opinion, I may adduce the marked infiltration of the lymphatics of the large blood vessels in Plate II, Fig. 5, and the fact—still more convincing—that, at least in several places, the earliest infiltration appears in the lymphatics. In a blood infection, one would expect the capillary region to be the first attacked; whereas, here, initial implication of the capillaries has been shown not to occur.

The conditions existing in rabies support my contention of the lymphatic spread of infantile paralysis. I proved that the changes in both diseases were completely in harmony; and that, from a pathological aspect, each had an equal right to be called an acute poliomyelitis. In rabies the spread of the virus was proved to occur by way of the nerves. But Homén, by his studies, has since shown that the way of the nerves is the path of their lymphatics.

Experimental investigations in monkeys have now practically confirmed the hypothesis of the lymphatic spread of acute poliomyelitis. It has already been mentioned that the disease can be produced by intravascular, subcutaneous, subdural, intracerebral, intraneural and intestinal inoculation. These various procedures, however, are of unequal value. The most reliable are intracerebral and intraneural inoculation.

How does the poison reach the spinal cord from an inoculation not infecting the blood? Most of the workers upon experimental poliomyelitis in monkeys have come to the conclusion that the virus spreads from the site of inoculation especially by way of the nerves; the infection extends along the lymphatics, which accompany the nerves. I can hardly do better than quote Leiner and v. Wiesner, who have directed special attention to this question: "In the vast majority of our experiments—omitting for the moment those which were intracerebral—we observed a definite relation between the site of the inoculation and the seat of the paralysis, analogous to that already established in inoculation experiments with tetanus. Flexner and Lewis, Levaditi and Landsteiner, and we, have already demonstrated that the inoculated extremity is the first to become affected with the disease. In proceeding with further experiments, we almost invariably proved that an inoculation in a nerve of a posterior extremity produced paralysis which was situated in, and tended to remain restricted to, the hind end of the body; and similarly, an inoculation in the median nerve primarily affected the fore part. Infection through the digestive tract causes paralysis of the posterior, that through the respiratory tract, of the anterior half of the body." These investigators conclude: "Our results, as a whole, indicate clearly that the seat of the paralysis depends upon the site of the inoculation; and that the virus of poliomyelitis reaches the spinal cord by the shortest route. We are thus able to con-

firm the view which we had previously stated and to which Römer and Kraus lent their authority, viz., within the organism the virus travels along the nerves, undoubtedly by way of the accompanying lymphatics. As what we have experimentally shown frequently occurs in accidental infections in man, these observations may be of importance in enabling us to determine the path of infection in human beings."

Landsteiner and Levaditi, by successful inoculation of the anterior chamber of the eye, and also by demonstrating that inoculation through the nasal mucous membrane renders the olfactory bulb virulent, have further established the probability that the nerves are the conducting channels for the virus.

As a control experiment Leiner and v. Wiesner clamped the sciatic nerve in an animal and injected the virus into the nerve distal to the clamp. They then thoroughly isolated and ligatured the nerve at the point where it had been clamped. Poliomyelitis did not follow the inoculation; the animal remained healthy.

Krause and Meinicke, contrary to other experimenters, assert that infection occurs through the blood stream; or, at least, that at a certain stage, a blood infection occurs. They actually found the blood and spleen of children, who had succumbed to infantile paralysis, contained the virus. Other investigators have failed to demonstrate the poison in the blood of infected monkeys.

The foregoing observations seem to add experimental ratification to the doctrine of lymphatic infection which I enunciated. Against this doctrine are two facts: first, that intracerebral inoculation may cause paralysis which sets in first in the lower extremities, and, second, that experimental poliomyelitis may be produced by intravenous injection.

Concerning the first, investigation is still being made: Leiner, Wiesner and Römer have already shown that here no essential contradiction necessarily exists.

Concerning the second, I think we must clearly distinguish between the way in which the poison reaches the spinal cord and the mode in which the changes of poliomyelitis originate. These are by no means one and the same. Let us take an elementary example. Suppose a certain amount of virus settles in, for instance, the region of the posterior horn. The changes which here occur produce no picture typical of the disease. If, however, the

poison spread to any extent, from the area first attacked, so that the characteristic appearances of acute poliomyelitis later develop, although the lesion in the primary disease focus in the cord be due to an infection by way of the blood, the subsequent and typical lesions certainly are not.

Leiner and v. Wiesner state that in monkeys, inoculation of the blood only exceptionally is successful. They have never, during the incubation period, been able to demonstrate the presence of the virus in the blood. Their observations sharply contrast with those of Krause and Meinicke who, as I have mentioned, state that in rabbits the most effective site of inoculation is the blood and who have demonstrated the virus in the blood, as well as in other tissues, during the initial stage of the disease.

Harbitz and Scheel arrive at a conclusion similar to my own, except that they maintain that the virus reaches the pia by way of the blood, and then invades the spinal cord along the sheaths of the vessel. Fr. Schultze, indeed, had already dwelt upon this possibility. He, however, considered it as an accidental phenomenon, which might happen in the course of a cerebrospinal meningitis, and which infrequently afforded an explanation of the characteristic pathologic picture, or of the symptom complex of the disease. Leiner and v. Wiesner, while not clearly recognizing the principal point of the problem—the peculiar localization, with marked participation of the gray matter, especially in the anterior horn—yet acknowledged the lymphatic origin of the morbid changes in the nerve substance. The double step in the infection seems to me not very probable; and microscopical examination fails to substantiate that the inflammation, as a rule, diffuses inward from the pia.

The point at which the virus enters human beings is still to be determined. Many different sites have been incriminated; *e. g.,* because of diarrhea in the initial stage, the alimentary canal was accused; because of angina, the throat; and because of bronchitis, the respiratory tract. Experimental research, especially by Römer and Joseph, proved that diarrhea might occur after intracerebral infection. Diarrhea, angina and bronchitis may, therefore, be accepted as consequent upon the elimination, and not upon the invasion of the virus. If it be permissible to deduce from animal experiments the mechanism of morbid changes in

human beings, then my belief that human infection takes place by way of the alimentary canal is not without foundation, for the paralysis almost always attacks first the legs and often remains confined to them.

Hoche believes the central canal of the nervous system plays a part in the pathogenesis, but it is difficult to understand the reason for his faith. If the morbid changes have any relation to the special infective process, presumably, a communication must exist between the site of infection and the central canal. Otherwise, only diffusion of the process within the spinal cord itself could be ascribed to the central canal. But the facts satisfactorily show that the central canal has no great importance. In some cases of acute poliomyelitis, elderly people in whom the central canal was obliterated, have been attacked; and in cases where the canal was patent, in and around it, extremely slight and not always definite pathological changes occurred. As in my early investigations, I paid special attention to the central canal and myself demonstrated these points. I consider there is no sound basis for Hoche's opinion. The tendency to attack children is peculiar to all infectious diseases and can hardly be connected with the patency of the central canal.

## CHAPTER IV

### SYMPTOMATOLOGY

*The General Clinical Aspect of the Disease.*—As a rule, Heine-Medin's disease begins quite suddenly, with fever and malaise. Tenderness is a frequent and prominent feature. Pain, headache, stiffness of the neck and spontaneous pains in the limbs appear. In some cases vomiting and diarrhea are present; in others, the disease commences with sore throat, coryza or bronchitis.

These symptoms, which are in no way peculiar to, or distinctive of, the disease, may constitute the whole clinical picture. After a few days the patient may recover without further symptoms: such is the typical course in abortive cases.

In others, again, after the malaise has lasted one or more days, paralysis appears. Paralysis is the only sign which is characteristic of the disease; and it is the only sign which conclusively establishes the diagnosis. Paralysis generally attacks the limbs—most often the legs—but it may also affect the trunk and head. It develops rapidly and within a few days attains its maximum extent and severity. In a number of cases complete recovery of function occurs, but usually in certain areas the paralysis diminishes to some degree and then remains stationary. It shows the characteristics of a flaccid paralysis, diminished reflexes, changes in electrical excitability, and atrophy. Subsequently, in cases in which the paralysis is persistent and extensive, paralytic contractures, faulty positions and deformity develop, and more or less incapacitate the patient.

According to the course of the disease, the seat of the paralysis, the predominance of isolated symptoms, and other features, I have distinguished the following forms of Heine-Medin's disease:

1. The spinal poliomyelitic form.
2. The form resembling Landry's paralysis.
3. The bulbar or pontine.
4. The encephalitic.

5. The ataxic.
6. The polyneuritic (resembling neuritis).
7. The meningitic.
8. The abortive.

Zappert gives the following classification:

1. Cases in which spinal paralysis preponderates (poliomyelitis in the restricted sense) with ultimate implication of the respiratory musculature (Landry's paralysis).

2. Cases with marked cerebral symptoms, especially referable to implication of the cranial nerves, more rarely, of the cerebral cortex.

3. Cases without special affection of the central nervous system, but with more or less marked meningeal, gastrointestinal or general febrile symptoms.

P. Krause differentiates:

1. Spinal form (poliomyelitis acuta).
2. Bulbar form.
3. Cerebral form: (*a*) Meningitic; (*b*) encephalitic; (*c*) ataxic (cerebellar).
4. Abortive form.
5. Recurrent or relapsing form.

Although I recognize that a simplification of my classification would be desirable, I cannot perceive that the grouping either of Zappert or of P. Krause marks any advance. They differ from one another: the ataxic Zappert includes with the bulbar, Krause with the cerebellar; the meningitic Zappert places in the same group as the abortive, Krause as the cerebral. Neither of these groupings seems to me to have much purpose. Indisputably, meningitic cases occur which prove fatal, and a whole series of cases run a course typical of spinal meningitis without affording any clinical evidence of implication of the brain. From my personal experience and from my intimate knowledge of recent literature, I believe that my classification is not only correct but also that its nomenclature gives the physician the best survey of the various clinical aspects of the disease. Zappert has acknowledged the didactic value of my classification. I might even assert that from my classification, one could picture the general features of the symptomatology of the disease.

*B. Details of the Initial Symptoms and of the Various Forms.*

(*a*) Heine-Medin's disease usually attacks those in perfect health and begins acutely with fever and malaise, speedily followed by paralysis. Many earlier observers have asserted that the paralysis develops without preceding symptoms. Occasionally mothers make similar assertions and allege that the child, having been well when put to bed in the evening, awoke the next morning with a paralyzed leg or arm. West created for those particular cases a special name, "morning paralysis." The wide experience of recent years has shown the extreme rarity of such cases. Careful inquiry reveals that most of those children present prodromal symptoms, which sometimes, however, are so slight as to evade notice till the attention of the relatives is specially directed to them. The cases in which sudden paralysis is alleged to happen occur chiefly among the very young. Older children and adults rarely give such a history. But veridical examples can be cited in which the initial symptoms were extremely slight.

Occasionally the disease begins so insidiously that a vague unwellness, without any positively localized signs, gradually develops. But, as a rule, after this ill-defined prodromal period, acute symptoms arise.

Occasionally, as the disease develops, an intermission occurs. The patient recovers more or less completely from the first attack, only to be re-attacked. This second invasion must be considered as a relapse, if in the interval the patient were quite well. Even when paralysis has been established, relapses have occurred.

The most constant symptom of the initial stage certainly is the fever. Simultaneous with the acute onset, the temperature, as a rule, rises rapidly. It usually reaches 38°–39°; according to Ed. Müller a temperature of 40°–41° Celsius may rarely occur. Generally, the fever is maintained for a few days or even a week, and it falls, either gradually with marked occasional oscillations, or rapidly, as in a crisis. Ed. Müller observed that the subsiding temperature did not reach merely a normal, but sometimes even a subnormal level, which persisted for a certain period. In some cases he noticed, almost always after four days, a second rise, which, in general, was associated with evident increase of the paralysis. Zappert reported cases in which the temperature persisted at about 40° for 8–14 days. I have rarely observed prolonged fever.

Wickman, and subsequently Ed. Müller, Zappert, Spieler, and others have especially emphasized that neither the height of the fever, nor the severity of the other initial symptoms, foretell the nature of the subsequent course. After mild initial symptoms, some patients develop extensive and severe paralysis; some even die. Others, after an alarmingly severe onset, soon recover, without a trace of the affection they have undergone.

Rarely the disease is ushered in by a rigor.

Besides the fever, there are other initial symptoms, such as headache and malaise, which have no special characteristics, but which may sometimes awaken suspicion. Drowsiness, general tenderness, stiffness of the neck and marked perspiration often appear. The drowsiness in most cases is very marked. Mothers frequently narrate that the patient has slept for several days and has awakened only to eat and to void. Spieler and several other observers have reported deeper disturbances of consciousness. Very rarely actual coma occurs; *sub finem vitae,* in lethal cases it may appear; complete unconsciousness may also arise, even in favorable cases. Zappert showed that coma may appear synchronously with the fever at the onset of the illness. Starr states that delirium generally accompanies the fever. Fürntratt recorded maniacal outbursts; and others reported delusions.

More characteristic than drowsiness is diffuse tenderness, which perhaps is the most noticeable symptom that in the initial stage directs our attention to the likelihood of Heine-Medin's disease. The mother notices that a mere touch is evidently painful to the child. Sometimes, if she only approaches the patient's bed, anxiety and protests are expressed by the little sufferer. The patient may hardly be able to tolerate either the pressure of the bed clothes or the same position for any length of time. In the early descriptions of the disease this tenderness which was known to Heine, Duchenne, and others, was scarcely mentioned. Medin emphasized its frequency and also its prominence in the clinical picture of the disease. Wickman, Starr, Zappert, Foerster, Ed. Müller, Netter, and others, confirmed his observations. This hyperesthesia is in many instances the most marked symptom in the initial stage. It is usually increased by passive movements, especially in my experience, by movements of the vertebral column, such as rising. Spontaneous pains exist, in some cases,

in the neck, back and extremities. Occasionally the pain has been observed to show itself only in the extremity which later becomes paralyzed. The pain is often excessive, and generally diffuse and continuous. Older patients sometimes describe it as radiating. Such pain usually persists only for a short time and disappears with the subsidence of the acute symptoms. It may, however, last for weeks and arouse a suspicion of neuritis.

Many cases on examination show an actual hyperesthesia of the skin, but others do not. This hyperesthesia, which, in my experience, is most marked over the spinal column, has its origin in the tenderness elicited by the movement. Again, in other cases, sensitiveness to pressure over the muscles and nerve trunks may be present and may persist, even as the spontaneous pain. Foerster, Spieler, and others have reported numerous cases of spontaneous pain in the limbs and pain on pressure over the muscles and nerve trunks. Byrom Bramwell demonstrated in several instances that the sporadic do not differ from the epidemic cases with regard to the occurrence of pain; and he pointed out that such pain is often mistakenly attributed to rheumatism.

I shall later consider objective disturbances of sensibility.

The explanation of the sensory irritability is somewhat uncertain. I, myself, am inclined to refer it to implication of the pia. But most observers tend to regard it more as a neuritic process. The possibility of such a process cannot be denied, but, at present, pathological evidence of its existence is lacking. I shall later return to this question; but the signs of irritation could undoubtedly be due to the meningitis, which is invariably demonstrable. To the changes in the pia a series of symptoms, usually ascribed to meningitis, are referable. In the mildest cases, only pain in the neck develops. Frequently, however, rigidity of the neck, demonstrable only on bending the head forward, is also present. Sometimes a distinct contraction may be observed; the head then is retracted. Head retraction may, however, be present without marked contraction of the muscles. Not seldom these symptoms are associated with pain and stiffness in the back; occasionally with orthotonus; more rarely with opisthotonus. In some cases, increased sensitivity of the spinous processes is present. Occasionally Kernig's sign has been noted (New York epidemic, Foerster, Ed. Müller); and occasionally the sciatic phenomenon (Wickman, Lindner and Mally).

Medin, Pierre Marie, Fr. Schultze and others have called attention to the occurrence of signs of meningeal irritation during the initial stage. Spinal infantile paralysis may therefore at the onset closely resemble meningitis. The frequency of these symptoms has only become known during the epidemics of late years.

The signs of meningeal irritation usually are evident, but not well marked. Sometimes, however, in the initial stage, they are so pronounced as to dominate the clinical picture.

Foerster has called attention to the reflex hyperextension of the vertebral column, which he frequently observed on attempting to raise recumbent children. He believes this sign to be somewhat characteristic of the disease. In Foerster's cases, and in Spieler's, the meningitic signs were unmistakable and persistent. Occasionally typical scaphoid retraction of the abdomen was also present (Foerster).

Starr, Krause and Ed. Müller state that sweating is an important early sign. Ed. Müller observed sweating quite at the onset or during the first days, in three fourths of his cases. Sometimes Müller's patients for weeks continued to perspire. Müller suggested the possibility, in such cases, of a lesion of the sweat centers or of their subdural tracts. Although I have not particularly referred to this sign in my own report, I can, however, confirm these observations; sweating is often profuse and its amount is not always dependent upon the height of the fever.

In early descriptions convulsions occupied a prominent place among the initial signs. Medin, however, stated that convulsions rarely occurred, except in cases which later proved to be encephalitic. In the epidemics I described, twitchings of individual limbs occasionally appeared, but convulsions rarely. During the Austrian outbreak Zappert observed convulsions and twitchings in the extremities among the early signs; he further noted that these signs were not restricted to the cases which later developed cerebral symptoms. Zappert does not state the seat of the irritation in these cases—if irritation of the cerebrum or of the spinal cord was responsible for these convulsive movements. During the epidemic in Hesse-Nassau, epileptiform seizures without unconsciousness, or spasms of a more tonic nature, were observed. Ed. Müller, however, noted only one case of severe epileptic convulsions with unconsciousness. In some cases, during the initial

stage, Wickman observed a tremor which was occasionally very marked, which resembled a mild intention tremor and which was absent in repose.

Quite frequently gastrointestinal disturbances appear at the onset. Vomiting, of no great violence, usually occurs alone; but intestinal disorders, sometimes constipation, oftener diarrhea, may also be present. The stools may be watery, green and fetid. Indeed, the diarrhea is sometimes such as suggests an acute gastrointestinal catarrh.

Medin, Wickman, Zappert, Krause and others have emphasized the frequency of gastrointestinal symptoms in the initial stage of acute poliomyelitis. Diarrhea is the usual manifestation; but in Spieler's cases and in the New York epidemic, obstipation was commoner.

Post-mortem examination has demonstrated that gastrointestinal symptoms arise from changes in the intestinal mucosa; swelling of the solitary follicles, of Peyer's patches, etc. Marie and some writers believe the changes in the intestinal tract to be symptomatic of a general infection; others consider the intestinal changes to be due to the primary action of the virus. Diarrhea in monkeys mostly occurs at the stage of paralysis. In man, the gastrointestinal signs appear as a rule at the onset of the disease and may precede all other signs of the infection. No one has yet been able to demonstrate the presence of the virus in the intestinal discharge.

The respiratory tract also may contribute symptoms to the initial stage. Ed. Müller reported the occurrence of respiratory symptoms in more than one half of his cases; some had severe persistent coryza; others sore throat, and a few conjunctivitis. But more frequent than these manifestations was severe bronchitis, which sometimes led the physician to diagnose influenza. Occasionally bronchopneumonia was observed. Römer, in several cases of initial angina, examined cultures from the throat and tonsils without finding any specific microorganism. In a proportionally great number of Eichelberg's cases, an initial affection of the air passages (sore throat, bronchitis, etc.) was observed. Lindner and Mally found in many cases marked fetor of the breath in association with the throat affection.

Skin eruptions, such as herpes labialis and varieties of ery-

thema, have been observed during the initial stage. Among one hundred cases Ed. Müller noted herpes thrice on the lips and once on the knee. Herpes is therefore rare. In other cases, he observed vesicular, measly, or scarlatiniform exanthemata. He also noticed similar appearances a week or more after the onset. The New York epidemic was peculiar inasmuch as skin eruptions occurred in 61 cases. The type of eruption was inconstant, but herpes appeared only twice. The rarity of herpes labialis is important in the differentiation of Heine-Medin's disease from cerebrospinal meningitis.

Very few other general symptoms have been observed. Isolated instances of swelling of one or more joints have been reported by Wickman, J. Hoffman, and Spieler. As the swelling was associated with general tenderness it was actually mistaken for acute rheumatism.

In rare cases, enlargement of the spleen has been noted (Ed. Müller).

Recently, Ed. Müller established the fact that leukopenia is tolerably characteristic of the initial stage of Heine-Medin's disease. He reported that in no instance either among fifteen cases in man, or among a series of infected monkeys, had he found an increase in the number of leucocytes during the febrile period. In the minority of the cases the count was normal, but in the majority only 3,000–5,000 leucocytes were present. Müller also proved that in monkeys leukopenia may occur long before the appearance of the paralysis and even in cases which remain free from paralysis. Krause, also, in such cases found leukopenia with a slight increase of lymphocytes. On the other hand, during a New York epidemic in six cases, leukocytosis ranging from 13,400 to 20,600 was reported. If further investigations confirm Müller's observations, the leucocyte count will prove a valuable aid in differential diagnosis.

In an epidemic the character of the initial symptoms may present much variety. During the Swedish epidemic of 1903, Wickman, however, observed that in a disease focus the general aspect of the initial symptoms might show considerable constancy. Thus, in one neighborhood, meningitic symptoms predominated; and in another, gastrointestinal. Exactly the same observation was made in the German epidemic of 1909. Ed. Müller, in the Hesse-

Nassau epidemic, observed severe intestinal symptoms only in the minority of cases, while Krause reported that about two thirds of the cases in Westphalia were initially afflicted with severe diarrhea. Yet Müller and Krause were reporting merely different foci of the same epidemic.

(*b*) *Paralytic Signs and Special Forms of Heine-Medin's Disease.*—In many cases only the onset of paralysis makes the diagnosis certain. Paralysis appears after the initial symptoms have lasted from one to several days. It is the sign most characteristic of Heine-Medin's disease. It may attack different parts of the body and may produce most diverse clinical pictures. The commonest type, the type which predominates in our conception of the disease, is the spinal, poliomyelitic form which is identical with the long-known infantile paralysis.

1. *The Spinal Poliomyelitic Type. Infantile Paralysis.*—The paralysis attacks mainly the extremities, and one or more limbs may be affected. The muscles of the trunk and neck in varying degree and combination, also, may be implicated. Cranial nerve palsies may occur in this type, but they are a negligible feature. Three stages of the disease may be distinguished: an acute stage, a stage of repair, and a chronic, definitive stage. Here I shall discuss the first two stages together and the chronic stage separately.

The paralysis either immediately follows the febrile stage, or, more commonly, develops during the course of the fever; increases rapidly in extent and severity and then partly diminishes, or, more rarely, completely disappears; and as a rule, is a purely motor paralysis of a flaccid type, with diminished muscular tonicity, muscular atrophy, and absence of reflexes.

Motor disturbances generally appear within the first three days. Very seldom complete paralysis is present from the beginning. Usually the initial signs are those of a palsy; the movements still preserve their normal range, but the muscles are markedly weak and easily fatigued. Adults are conscious of the progressive development of their muscular weakness: children may complain of it; or their elders may note the increasing feebleness of the child's attempts to move in and out of bed. In infants and little children the paralysis is usually not observed until it is far advanced: even then to determine its nature is often difficult. In infants who have not yet learned to walk a diagnosis may some-

times be more easily reached by observing the lack of resistance to passive movements, the flaccidity of the muscles and the loss of reflexes, than by relying upon the absence of active movement which, of course, on more prolonged observation will also be evident. It must be borne in mind, however, that consequent upon the attempt to elicit a deep reflex in a child, an inhibitory degree of muscular tension may be induced, and thus a loss of reflex may be simulated. Sometimes great patience, therefore, is necessary to determine whether a reflex actually exists or not. Special care is needed when spasm of the muscles is present, or when no normal standard remains owing to the real or apparent loss of the reflex on the first examined side. The motor functions of the body become more limited as the paresis advances. If the legs are affected, the child may perhaps be able to move them in bed; but if he attempts to stand, he collapses; to walk now is for him impossible. If only one leg be attacked, the child, still able to stand upon the healthy leg, falls if he tries to support himself upon the affected leg. But occasionally one is deceived in this experiment by children who maintain their upright posture upon the weakened limb by hyperextending it at the knee joint so as to immobilize and fix it—just as if it were a wooden leg. The strength of the arms may also be reduced and the normal range of movement lost. If movement be retained, it is limited in range and so feeble in power as to be prevented by very slight resistance.

If the paresis progresses, complete paralysis results and the afflicted extremites become motionless. Later, a slight motility may be observed in a few muscles. When the paralysis affects several limbs, as a rule muscles of the trunk also are affected, and the neck muscles, too, may be implicated. A patient in such a condition presents a pitiful picture of helplessness. He is a mass without motion. When he is lifted out of bed, his head and limbs loosely hang suspended as pendulums. In a few cases, even if the paralysis be extensive, it more or less completely disappears, occasionally within a very short time.

Neurath observed a case in which the usual rapid development and subsequent amelioration of the paralysis were absent; instead, a sudden onset was followed by a progressive course for a few months. It seems to me to be improbable that this case was

really an example of Heine-Medin's disease. Foerster, however, observed cases where the paralysis reached its maximum extent only after 12 days.

*Character of the Paralysis.*—Before I discuss the localization of the paralysis, I shall first refer to its characteristics. Typically, the paralysis is flaccid and is associated with loss of reflexes, hypotonicity, changes in the electrical irritability and atrophy.

Usually, the reflexes disappear. Medin, however, showed that in sporadic cases the knee jerk may even be increased. Later investigators have also reported variations in the reflexes. As the legs are most commonly affected, let us first discuss the alterations of the knee jerk.

1. *Absence of the knee jerk* is the rule. It is noteworthy that the loss of the patellar reflex may be the only demonstrable objective sign of the disease (Wickman, Ed. Müller, Zappert).

2. An initial increase with subsequent disappearance may occur (Wickman, Ed. Müller).

3. If the arm be affected, or if the bulb be implicated, an otherwise normal leg may show an increase of the patellar reflex (Wickman, Neurath, Zappert, Foerster, Ed. Müller).

4. Paralysis and loss of reflexes in one leg may be associated with apparent healthiness and increase of reflexes in the other (Wickman, Zappert).

5. The patellar reflexes may be increased in a paralyzed and obviously atrophied leg (Wickman).

These variations cannot with certainty be interpreted. The initial increase with subsequent diminution may I think be explained by supposing that in the earlier stage of the disease the inflammatory process increases the irritability of the spinal cord. As the disease advances the stimulation gives place to the destruction of nerve cells and this irritability diminishes till the reflexes disappear.

More interesting are the cases in which an increase of the leg reflexes coexists with flaccid paralysis of the arm of the same side, or with a lesion at a still higher level. Evidently, the pyramidal tract, in its course through the segments of the affected cervical cord or bulb, is injured, but to so slight an extent that the injury is manifest not as a paralysis of the leg but only as an increase of its reflexes. Ankle clonus also may be observed in such

cases (Wickman, Neurath). Foerster found this sign in the very acute stage.

These observations are important, as, also, are those of the sensory disturbances which will later be mentioned, because they together constitute the clinical expression of the localization of the morbid changes.

The same explanation may suffice for categories 3 and 4.

Increase of the knee reflex accompanying paralysis of the leg seems almost inexplicable. In the very rare cases which show this phenomenon implication of the pyramidal tract at a level higher than that of the lesion causing the atrophic paralysis, must give rise to an overcompensation of the reflex excitability of the paralyzed limb.

Other tendon reflexes, also, undergo corresponding changes. Usually, in paralysis of the leg, the tendo Achillis reflex disappears; and in paralysis of the arm the arm reflexes are lost. Varying reports exist upon the nature of the tendo Achillis reflex in this disease; according to Zappert, in the same extremity, absence of the knee jerk is not seldom associated with increase of the tendo Achillis reflex. Occasionally the arm reflexes may be exaggerated (J. Hoffmann).

Oppenheim has reported a case which shows how the tendon phenomenon may differ even in the same patient. The shoulder muscles were paralyzed on the left, the quadriceps on the right, and the sural triceps, the peronei and the extensor communis digitorum on the left. The tendon reflexes were as follows: Absence of right knee jerk; right tendo Achillis reflex distinctly, even markedly, present; left knee jerk conspicuously present; but left tendo Achillis completely absent.

The superficial reflexes also may disappear. Wickman and, later, Lindner and Mally reported that the abdominal reflex even in pronounced paralysis of the abdominal muscles is preserved. Babinski's sign, also, has been observed. Strange to say, Foerster found it present either on one or on both sides in all cases; it was not continuously demonstrable but disappeared occasionally only to return; at times it persisted for a month.

The affected limbs are markedly hypotonic. The hypotonicity does not show itself only by abnormally slight resistance to passive movements, but also by a flaccidity of the muscles to touch

which sometimes exists in limbs in which no paresis can be detected. Hypotonicity is often an invaluable aid to diagnosis. In little children this sign, especially when associated with loss of reflexes, is of great value, for paralysis and still more paresis is often difficult to establish in them. But hypotonicity, however, is not of invariable occurrence. Occasionally, in a paretic limb, one group of muscles may be hypertonic.

A further important sign of paralysis in the spinal type of Heine-Medin's disease is alteration in the electrical irritability of the muscles. These electrical changes appear mostly during the course of the second, occasionally even toward the end of the first week. Jagic's case, which was confirmed microscopically, showed normal faradic excitability eighteen days after the onset. The change may be merely quantitative, a decrease or complete loss of irritability to faradism. A partial or complete reaction of degeneration may develop.

After the illness has lasted for several weeks, a more or less pronounced atrophy of the paralyzed muscles gradually appears. It progresses more rapidly and markedly in the muscles which later remain paralyzed. The atrophy is caused not only by the trophic disturbances, arising from the changes in the nervous system, but also in part by disuse.

*Distribution of the Paralysis.*—The paralysis in different cases greatly varies in its extent, its combinations and its forms. It has been proved that the legs are most frequently affected, and that no muscle area is secure from attack.

During the Swedish epidemic of 1905 the distribution of the paralysis was as follows:

| | Cases. |
|---|---|
| 1. Paralysis of one or both legs | 353 |
| 2. Paralysis of one or both arms | 75 |
| 3. Combined paralysis of leg and arm | 152 |
| 4. Combined paralysis of leg and trunk | 85 |
| 5. Combined paralysis of arm and trunk | 10 |
| 6. Isolated paralysis of trunk muscles | 9 |
| 7. Paralysis of the "whole body" | 23 |
| 8. Ascending paralysis | 32 |
| 9. Descending paralysis | 13 |
| 10. Combined paralysis of spinal and cranial nerves | 34 |
| 11. Isolated paralysis of cranial nerves | 22 |
| 12. Localization of paralysis not mentioned | 60 |
| | 858 |

Probably only the first two categories are accurately counted; the figures relating to the lower extremity affections are especially reliable. The number of the combined paralysis of arm and leg, however, is, in my opinion, too high. When I had an opportunity to examine such cases in the early stage of the attack, I found that in addition to the affection of the arm and leg, the trunk muscles, especially the abdominal, were implicated, also. In category 6 I included 3 cases of paralysis, confined to the neck muscles. Category 7 comprises cases which might just as well be included in 4 or 5, and others, also, which might be classed with the ascending or descending paralysis. Finally, as many of the cases in 8 and 9 had cranial nerve palsies, they could be referred to category 10. The figures show that the legs are most frequently attacked. In 353 out of 808 cases, 43.69 per cent., paralysis was confined to the lower extremities. If we now add together the cases in which one or both legs were involved (all, in categories 3, 4, 7, 8, 9; and 24, in category 10), we find not less than 692 cases out of 808—85.64 per cent.—in which the lower extremity was attacked. Analogous results, with slight variation, occurred also in other epidemics. Leegaard found paralysis confined to one or both of the lower extremities in 58.2 per cent. of 311 cases; whereas, in 83.6 per cent. (260 out of 311) the lower limbs were implicated alone, and in association with other areas. Ed. Müller stated that in four fifths of all cases the lower extremities were attacked. In Medin's epidemic, a similar incidence of the paralysis prevailed. In discussing the relation of epidemic to sporadic poliomyelitis, mention might have been made of the fact that the earliest observations of the disease emphasize the frequency with which the legs are affected.

Lovett and Lucas, in 628 polyclinic cases, found both legs affected in 130; right leg, in 216; left leg, in 239; right arm, in 5; left arm, in 5; all four extremities, in 3; both legs and one arm, in 2; trunk muscles with other area, in 6; in 15 hemiplegia existed, and in 7 crossed paralysis. In order of frequency, paralysis of the arm is generally believed to follow paralysis of the leg. Müller, however, states that affection of the trunk is more frequent than of the arms and is second only to that of the legs. He noted in over two thirds of his cases that the trunk muscles were implicated.

Paresis of the trunk muscles always accompanied severe paralysis of the lower extremities, but was usually transient. Zappert calls attention to the fact that in his experience the left side was surprisingly more often attacked than the right: arm palsies—8 right, 16 left; leg palsies—29 right, 38 left; hemiplegia—8 right, 14 left. During the New York epidemic, 29 left, 21 right arm palsies; 171 left, 120 right leg palsies, and 15 left and 16 right hemiplegias were reported. I myself found 34 left, and 24 right arm palsies; 61 left, 60 right leg palsies and 9 left, and 23 right hemiplegias. Leegaard gives the following figures: Arms, 21 right, 21 left; legs, 36 right, 44 left; hemiplegia, 7 right, 8 left.

It is evident that every part of the spinal cord may be attacked in this affection. Clinically, the disease occasionally seems to be confined to a circumscribed area. The great variability of the paralysis is obvious not only when the whole body is attacked, but also in infections involving single limbs. In the extremities, even during the first period, when the paralysis is of greatest intensity and extent, accurate observation seldom reveals a complete mocoplegia or paraplegia. Even when the whole leg lies motionless, the toes may still be capable of movement which, however, is more weak or less free than normal. An analogous condition occurs not rarely in the arm. After some time has elapsed, the unequal distribution of the paralysis is more evident. Although a great variety of combinations of paralysis may develop, certain types appear more often than others. In the leg, the peroneal group and certain muscles of the thigh—in my experience the quadriceps femoris especially—tend to be implicated. Although the paralysis seems to be localized to these muscles, others are to some degree affected also. Lovett and Lucas showed that in not less than 355 out of 478 cases in which the legs were implicated, the quadriceps either alone or in combination with other muscles was affected. Next in frequency to the quadriceps, comes the tibialis anticus, which is oftener attacked than the peroneal group. Of the flexors of the thigh, the mesial muscles are more frequently paralyzed than the lateral. In the upper extremity, an analogous condition exists; *i. e.*, in frequency and distinctness, paralysis of the deltoid and of the upper arm preponderates (E. Remak).

Sometimes the motor disturbances assume the form of an

upper or lower plexus palsy (Oppenheim, Cestan and Huet, Déjerine, Cruchet, etc.).

The experience that the proximal parts are the more severely attacked, is in accord with the observations of early writers, such as Seeligmüller, Baumanns and others. Cases occur, however, in which the distal are more implicated than the proximal parts. Very often, according to Ed. Müller, second in frequency only to the affection of the legs, when severe paralysis exists, the trunk muscles are involved. The patient then may not be able to turn in bed or to change his position without help. The paralysis of the muscles of the back prevents sitting up in bed. When made to assume an upright position, the patient falls forward or to one or other side. From a bending forward attitude the patient cannot sit upright. Later, in consequence of the paralysis of the back muscles, scoliosis and kyphosis may be especially marked. If the abdominal muscles are attacked, the patient cannot rise from a recumbent position. When an attempt to rise is made the abdominal muscles remain quite flaccid; and the abdomen protrudes during the effort owing to the contraction of the diaphragm upon the intestines. In the acute stage, as the paralysis is usually bilateral and diffuse, all the muscles of the abdominal wall, as a rule, are attacked. But cases occur in which the paralysis is only unilateral: a protuberance of the abdomen then appears upon the paralyzed side, and the umbilicus is drawn to the healthy side. Rarely, after the disease has lasted some time, only isolated muscles may remain paralyzed, and a circumscribed hernial protuberance of the abdominal wall then appears which often closely resembles a lumbar hernia. Duchenne mentioned this implication of the abdominal muscles in acute poliomyelitis, but Medin, Ibrahim and Herrmann, Oppenheim, Wickman, Petrén, Ed. Müller, Foerster and others particularly studied it. Strassburger and Foerster report cases in which the only motor disturbance was paralysis of the abdominal muscles. In Foerster's cases, this paralysis was associated with obstinate constipation which he considered was due to a paralysis of the intestinal muscles, secondary in some cases to that of the abdominal muscles.

Ed. Müller noted that the abdominal muscles were affected next in frequency to the legs. This is of interest to me as it shows that even in non lethal cases conditions prevail which re-

semble exactly those which I have established in fatal cases, namely, that the changes in the spinal cord during the early stage are continuous and extend longitudinally. Generally, the paralysis of the trunk later disappears and the disease often assumes the outward semblance of a disseminated myelitis.

The respiratory muscles may also be involved. The intercostal muscles are more frequently affected than the diaphragm. Paralysis of either produces functional disturbance which, in my experience, is especially marked when the diaphragm is paralyzed. When the attack falls upon the intercostal muscles, the chest may slightly move or remain motionless. Breathing may be carried on exclusively by the diaphragm.

The intercostal paralysis is generally bilateral, but, as Medin, Foerster and Spieler observed, it may be unilateral.

The functional disturbances resulting from paralysis of the diaphragm are marked and characteristic. The epigastrium during inspiration is drawn in; during expiration, protruded.

Paralysis of the respiratory muscles is of special importance for prognosis. If the intercostal muscles and the diaphragm are severely attacked, danger of asphyxia threatens; and the existence of an affection of the respiratory muscles later predisposes to pneumonia.

Not rarely the neck muscles are affected. They are oftener implicated in the ascending type of the disease. The functional disturbances are characteristic if the flexor and extensor muscles are attacked; the patient cannot lift his head from the pillow; when he is raised his head and legs hang down backwards; if his body is bent a little forward, his head falls forward or to one or other side and, controlled only by gravity, remains completely passive. This paralysis of the neck is usually accompanied by paralysis of the extremities, but during the Swedish epidemic of 1905 at least 3 cases of isolated paralysis of the neck muscles occurred. Wickman in the Stockholm epidemic of 1899 reported another case in which only the neck muscles were affected; this case was interesting for, as it showed increased knee jerks and ankle clonus, the pyramidal tracts were probably injured in their course through the cervical cord.

Erb classified as acute superior-anterior poliomyelitis those cases in which the disease is situated in the cervical region of the

cord as high as the first cervical segment and partly invades the medulla oblongata to attack isolated cranial nerves. Foerster had previously described this form.

Oculo-pupillary signs such as narrowing of the palpebral fissure and contraction of the pupil have occasionally been observed (Wickman, Oppenheim, J. Hoffmann, Spieler, Lindner and Mally).

*Rectal and Bladder Phenomena.*—Although Heine observed that a temporary weakness of the bladder and rectum might occur, it was supposed that bladder disturbances did not arise in infantile paralysis. Medin, however, during the fever stage of several cases, observed retention of urine, which occasionally demanded catheterization. During the Swedish epidemic of 1905 I recognized many cases of retention, but only isolated examples of incontinence of urine. Zappert, also, has reported bladder disturbances. Ed. Müller considers that they are among the commonest of the signs of the early stage of the disease and that their frequency is underestimated because they are so transient and slight. They soon disappear and only rarely persist for any length of time. These disturbances of micturition may be a febrile epiphenomenon; but, as among children who have already learnt to control their sphincters, such disturbances seem to be commoner in Heine-Medin's than in any other infectious disease, I believe they more probably are due to changes in the nervous system. Moreover, their organic nature is confirmed by their long duration in quite a series of cases and by their almost exclusive association with paralysis of the legs (Krause and Ed. Müller). Spieler, however, observed persistent severe retention of urine associated with paralysis of one leg, and Peiper reported a case in which it was associated with paralysis of an arm. Oppenheim considers that the rare occurrence of sphincter paralysis in this disease favors the view of L. R. Muller that the centers for the bladder and rectum lie not in the spinal cord but in the sympathetic ganglia. Foerssner, Sjovall, and others, also, have reported sphincter trouble in Heine-Medin's disease. As the ganglion cells often are slightly or not at all affected, whereas the interstitial tissue usually suffers severely, the evanescent nature of the bladder disturbances may perhaps be deemed in harmony with the anatomical change. The transient bladder troubles are probably analogous to the fleeting muscular palsies already discussed.

*Sensibility.*—Generally, poliomyelitis shows no objective disturbances of sensibility. However, there are a number of cases known where sensory disturbances were proved. Medin observed a child who had a transient complete anesthesia of the legs. A similar case was noted by Krause. A patient of Wickman showed a distinct diminution of sensibility to pain over the legs; the temperature sense in this case was also impaired and it persisted unimproved for at least one year after the commencement of the illness. Diminution of sensibility to the faradic current has been reported by Vulpian, Seeligmüller and Oppenheim. Wickman observed that this disturbance very regularly occurred and that it was not associated with any other impairment. Ed. Müller thought that in adults he could demonstrate at the beginning of the disease a widespread diminution of sensibility, mainly to pain and temperature; he alleges that this analgesia is very common in the initial stage, but that on account of its transient character, and of the early age of most of the patients, it generally escapes observation. In one of his cases the sensory changes were marked. Dissociated disturbances of sensibility imply a posterior horn lesion—an implication in harmony with pathological findings.

*Cerebrospinal Fluid.*—The marked meningitic symptoms and the constant round-cell infiltration of the pia lead us to anticipate some deviation from the normal in the cerebrospinal fluid. Müller invariably found the fluid to be at high pressure, even a few weeks after the beginning of the disease. The fluid was clear and quite sterile; its albuminous content was increased; the addition of silver nitrate gave distinct indications of chloride; the cell content consisted of lymphocytes so few as not to be visible as a sediment on centrifugalization. Wollstein obtained practically the same results. Other investigators, Guinon and Paris, Triboulet and Lippman, Achard and Grenet, Brissaud and Londe, Starr, Petrén and Ehrenberg, reported an increase in the number of lymphocytes. Leucocytes as well as lymphocytes have been found in some cases, but only very exceptionally (Raymond and Sicard, Netter) were the leucocytes in the majority. The results of cytological examinations correspond therefore with the microscopical investigations, which showed a lymphocytic infiltration of the pia. In isolated cases (Spieler and Netter), the clear fluid on standing coagulates.

In the chapter on etiology I have already discussed the results of bacteriological investigation of the cerebrospinal fluid.

In several cases, Wollstein, and Römer and Joseph studied the complement fixation properties of the cerebrospinal fluid, but obtained negative results.

*Final or Atrophic Stage.*—Reference has already been made to the occurrence of partial or even of complete disappearance of the paralysis. The period within which, under proper treatment, involution or recovery is still possible, is about one year, or, according to some authors, even longer. Finally a time arrives when the existing paralysis remains stationary. The disease has then attained the chronic or final stage. Heine, Duchenne, Charcot, Seeligmüller and others exhaustively studied this stage.

In addition to the changeless paralysis and the atrophy of muscles, secondary phenomena, such as deformities, alteration in the bones and joints, anomalous development, and vasomotor disturbances characterize this stage. Atrophy of varying degree is present in the permanently paralyzed muscles. Occasionally this atrophy is cloaked by a pseudohypertrophy. But the atrophy and the consequent change in the configuration of the limb is generally obvious.

Fibrillary twitchings have occasionally been observed in the atrophic muscles (J. Hoffmann).

The most frequent deformity is pes equinus, which, in patients confined to bed, arises from the drooping of the foot and the pressure of the bed clothes. Reducible at first, the foot later becomes fixed by retraction of the muscles. The contracture of the non-paralyzed flexors of the foot aggravates the deformity.

The pes equinus may develop gradually from an attempt to compensate for the diminished growth of the affected leg.

More rarely than pes equinus, pes varus results. Quite frequently the deformity is neither a pure pes equinus, nor yet a pes varus, but an equino-varus. Pes valgus and pes calcaneus also may develop. I shall not discuss the origin of these deformities, nor the bone and joint changes, for they more closely concern the orthopedist than the neurologist. These deformities disclose that the paralysis does not affect all the muscles of any group. When muscle groups are completely implicated, loose joints result especially at the ankle, shoulder or hip.

At the knee joint hyperextension may occur and produce a more or less distinct genu recurvatum. Hyperextension is often detectable in cases in which the paralysis is very slight; in my experience it is without diagnostic importance. More rare than genu recurvatum is genu valgum or genu varum. In certain cases a flexor contracture develops at the knee joint. A great number of patients present scoliosis. The scoliosis may be static—sec-

FIG. 2. Spinal form of poliomyelitis with paralyses and atrophy of the left arm since childhood. (The muscles of the shoulder girdle mostly involved. After Bryom Bramwell.)

ondary to a paralysis and shortening of a leg—or it may be a sequel to a partial paralysis of the back muscles. Messner, Kirmisson, Vulpius and most other investigators state that the con-

vexity is generally directed towards the healthy side. Carles, however, has described a number of cases where the convexity was directed towards the affected side. In spite of the many investigations of scoliosis, its mechanism has not yet been explained. Lordosis may arise from paralysis either of the back muscles or of the abdominal muscles and kyphosis may also occur but both are rarer than scoliosis.

If—as seldom happens—the neck muscles be only partially paralyzed, a torticollis may arise from contracture of the sternocleidomastoids of the healthy side.

Although contractures and deformities have gradually passed into the realm of orthopedic surgery, they yet merit minute attention from physicians and neurologists who alone are in a position to prevent their development. The avoidance of these deformities is of prime importance for they tremendously increase the difficulty of the surgeon's task. The accompanying pictures depict the extent to which such deformities may exist.

If the extremities be severely affected, their growth is generally retarded. Heine demonstrated by palpation that in this disease the bones may become atrophied; recently his observation has been confirmed by means of X-ray examination by Johannesen, Achard and Levi, Oppenheim and others.

In a few cases, however (Seeligmüller, Kalischer, Neurath, Oppenheim), an elongation of paralyzed extremities has been observed. Various explanations have been given of this paradoxical behavior of the bones. Seeligmüller supposed that the freedom from use might promote elongation, whereas Kalischer blamed trophic influences. According to Neurath, the elongation is only apparent and transient; only rachitic children suffering from recent poliomyelitis are said to show it; in them, if the paralysis be unilateral, the rachitic process—which retards growth—is made more obvious in the non-paralyzed limb. The growth of the paralyzed leg sometimes is surpassed by that of the non-paralyzed leg only after the rickets has disappeared.

Vasomotor disturbances manifest themselves in cyanosis and in lowering of the surface temperature. Heine described these changes and showed that the difference of temperature between the paralyzed and sound extremity might be considerable.

Higier, in a few cases, noted a striking dryness restricted to the skin of the paralyzed extremities.

Another vasomotor change, first observed by Oppenheim, is an indurated edema, which may be so marked as to simulate an hypertrophy of the paralyzed leg.

Among other anomalies of Heine-Medin's disease, Oppenheim mentioned immoderate development of the penis and the precocious appearance of hair upon the mons veneris in the young.

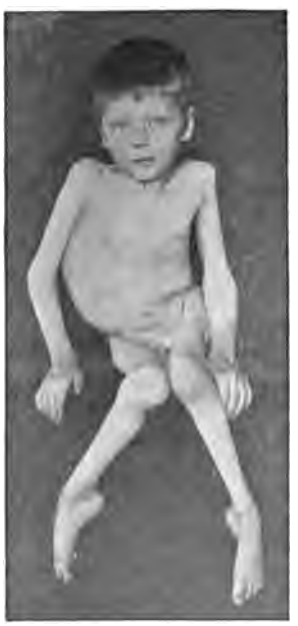


FIG. 3.

FIG. 4.

FIGS. 3–4. Spinal form of poliomyelitis with extensive paralyses and deformities. (After Johannessen.)

*Relapses.*—The initial symptoms—as I have already said—may develop in two relays. The second relay, as if it were a relapse, occasionally occurs after the patient has recovered from the first. Paralysis may also follow an analogous course. Medin, Auerbach, Leegaard, Neurath, Foerster and Schwartz (New York epidemic) and others have mentioned such cases. The interval between the attacks may be weeks or months. These relapses contradict clinical, epidemiological and experimental experience which indicate that a single infection produces immunity.

## CHAPTER V

### SYMPTOMATOLOGY

### *The So-called Landry's Paralysis Type*

Reference has already been made to distinct and continuous progression of the paralysis from one part of the body to another. If in such cases respiratory disturbances arise, death follows fast and a symptom complex, known to literature as Landry's paralysis, thus evolves.

In 1859, Landry described a disease, characterized by flaccid paralysis, beginning in the legs, progressing upwards and terminating in respiratory paralysis. Sensibility remained intact or was only slightly diminished; the electrical reactions were unaltered, and the post-mortem findings were negative. The last two features were later disproved. In an array of cases, microscopical examination demonstrated morbid changes—usually a multiple neuritis or acute myelitis, occasionally an acute poliomyelitis (Immermann, Mönckeberg, Schmaus).

Later Wickman showed that the fatal cases of acute poliomyelitis ended in exactly the same clinical picture as Landry's paralysis and that many cases, which were recorded as Landry's paralysis with myelitic changes, were merely acute poliomyelitis. These statements were corroborated in subsequent epidemics.

This type affects mostly the leg. After initial general symptoms, paralysis in the legs develops and progresses upwards to attack first the muscles of the abdomen and back, then the arm and neck, and finally bulbar symptoms appear. Cranial nerves are attacked, and as the respiratory center is implicated, dyspnea appears. Death occurs on the third or fourth day. Generally, consciousness remains clear until the very end; more rarely, coma precedes death; occasionally, Cheyne-Stokes' respiration appears. Sensibility is either normal or only slightly reduced.

If the disease progresses so far as to produce respiratory disturbances the issue is usually fatal. If recovery does take place, signs of a widespread spinal type of the disease occasionally associated with paralysis of isolated cranial nerves persist.

Rarer than the ascending is the descending type. According to Landry's original description, the symptoms appear in the region of the bulb and thence extend downwards. This descending type is very rare. But such forms as begin in the arm, attack then the leg and finally the bulb. Forms intermediate between ascending and descending paralysis are usually classified as "descending." Occasionally the legs may be spared altogether, and the arm paralysis be immediately succeeded by respiratory difficulty. The patient then quickly sinks.

This progressive course with terminal disturbance of respiration is most evident in adults, as they can themselves observe the advance of the disease. Most lethal cases so evolve. In older children the progress may readily be traced; in those of tender years the difficulty of following the evolution is naturally greater, but not insurmountable.

The negative results originally obtained on electrical examination by Landry have been corroborated; such patients generally die before electrical changes have time to develop.

During the Swedish epidemic of 1905, of 159 patients who died during the first two weeks, 45 conformed with the picture of Landry's disease (32 ascending, 13 descending paralysis). As most of the fatal cases were not described in detail but were reported only as having shown widespread paralysis, these figures are too low. I do not mean that this is the only mode of death in poliomyelitis. The meningitic symptoms may predominate, but such cases are more rare. In the Austrian epidemic, among 29 deaths, Zappert found 14 cases of Landry's paralysis. He stated that older children were so attacked; whereas, among children under five years of age, cerebral signs predominated. Zappert's experience may have been peculiar to the epidemic he observed; I am, however, of the opinion that the difference in great part depends not upon variations in the course of the disease at the several age periods, but upon the greater ease with which the course can be determined in older individuals.

That fatal cases usually run a course resembling Landry's paralysis is amply corroborated by numerous reports from the latest epidemics.

3. *The Bulbar (Medin) or Pontine Type (Oppenheim).*—If we ignore isolated observations (Eisenlohr) not quite free from

objection, Medin was the first to mention the involvement of the cranial nerves as a not uncommon complication of infantile paralysis. He further recognized the etiological connection of certain isolated cerebral nerve palsies with infantile spinal paralysis.

In discussing the spinal type, it has been mentioned that not infrequently the cranial nerves are attacked. Either the spinal or the cerebral component may be emphasized in the clinical picture. Sometimes the cerebral may be so transient and ill defined as to rank only as a complication of the spinal symptom complex. Sometimes the spinal is the less obvious and symptoms of involvement of the bulb or of the brain stem predominate. There is, however, no sharp line of demarcation between these two components; in a case of Ed. Müller, for example, a facial palsy coexisted with marked hypotonia of the muscles and loss of knee jerks on one side.

Yet there are cases which show only symptoms of infection of the bulb, pons, or brain stem—the bulbar, or pontine type. The seventh nerve is the most frequently attacked and as a rule the

FIG. 5.

FIG. 6.

FIGS. 5–6. Bulbar form of poliomyelitis with paralysis of the left facial and the left hypoglossus.

upper as well as the lower branch is implicated. The paralysis may be combined with atrophy and loss of electric excitability (Wickman and Oppenheim). The prognosis of facial palsy in this disease is usually good. The paralysis may be only partial; complete or practically complete recovery may then ensue. The

facial palsy, which appears as a complication of the spinal type of Heine-Medin's disease, seems to have an especially good prognosis. Wickman showed microscopically that such transient palsies depend upon a not inconsiderable nuclear affection. As a rule the facial paralysis is partial; rarely has an affection of both sides of the face been observed (Medin, Ed. Müller). Spieler described a case where the facial paralysis was associated with a homolateral disturbance of taste.

In several cases the paralysis of the seventh was associated with paralysis of the hypoglossal. The affected half of the tongue was flaccid to the touch; later, it atrophied. The patient had a feeling of difficulty in moving the tongue. Unilateral paralysis of the hypoglossal does not, however, cause much inconvenience. So far as I know the recovery of a case of bilateral paralysis has not yet been reported. Bilateral hypoglossal paralysis may have occurred in fatal cases in which paralysis of swallowing was present.

Paralysis of the abducens and of the oculomotor nerve is not uncommon. The abducens in my experience is more frequently affected than the oculomotor. Medin and Wickman have reported cases of paralysis of both the abducens and the oculomotor in which ultimately the trochlear shared so as to produce a more or less complete ophthalmoplegia. The paralysis is generally partial. During the epidemic in Breslau, in 1909, I saw, however, in Czerny's clinic for children, a child affected by bilateral external ophthalmoplegia after a short initial stage in which sweating was conspicuous. The completely motionless eyes were directed forwards; distinct though partial ptosis was present on both sides, but accommodation and convergence were preserved. Takahashi reported an analogous case in the Vienna epidemic: paralysis of the external oculomotor and of the trochlear nerves on both sides was present, together with a slight paralysis of the facial and of the left hypoglossal.

In cases of unilateral ophthalmoplegia the seventh fibers to the levator palpebræ were unaffected. Yet, in Heine-Medin's disease, ptosis may occur and may be the only sign of affection of the eye muscles. Nystagmus occasionally may also be observed (Medin, Ed. Müller, Netter).

I may appropriately here mention that the optic nerve also is

in rare cases affected. Tedeschi found complete blindness with optic atrophy in the left eye of a chronic case and Wickman demonstrated optic neuritis in a recent case. Ed. Müller, however, found the fundus always quite normal.

As observed by Medin, Wickman, J. Hoffmann, Lindner and Mally, implication of the trigeminal may cause a paralysis of the jaw muscles.

The ninth, tenth and eleventh nerves may also be affected. In several, mostly fatal, cases difficulty in swallowing was present, but isolated paralysis of the pharynx has also appeared in a few cases. Wickman recorded as the only symptom in one case, a unilateral paralysis of the velum palati. If the palsy is incomplete, the injury to the muscular apparatus may still be recognized from the striking tendency of the patient to swallow "the wrong way."

Involvement of the laryngeal muscles may produce hoarseness or aphonia (Medin, Huet, Wickman, J. Hoffmann). Respiratory disturbances may depend upon either an affection of the center for the intercostal muscles or a lesion of the nucleus of the vagus. It is sometimes impossible to distinguish the precise origin of the disturbance. One kind of respiratory disturbance, which in all probability is due to involvement of the vagus, is the spells of respiratory difficulty described by Wickman and Medin; tachycardia accompanies these spells.

Cheyne-Stokes' respiration, which has been observed in a few cases, is certainly due to an affection of the respiratory center. I have already mentioned a case in which the accessorius almost alone was involved. During the epidemic in Sweden, in 1905, paralysis localized to the neck muscles was noted in a few cases. Besides these paralyses of cranial nerves, the bulbar type of Heine-Medin's disease sometimes presents symptoms which arise from implication of nerve tracts which merely pass through the brain stem or bulb. Wickman described such cases; in one, besides paralysis of the eye muscles and of the left side of the face and right side of the tongue, cerebellar ataxia was present; another showed paralysis of the left facial and hypoglossal, slight scanning, syllable-stumbling speech, some ataxia of the arms and exaggeration of the deep reflexes of the legs. Zappert and Spieler enumerate analogous cases. J. Hoffmann observed in two cases

dizziness which he thought was of bulbar pontine origin. The following figures may serve to show the frequency of cranial nerve affections. Medin found among 64 or 65 cases, nine cases of involvement of the facial, in three of which no other symptom of the disease was present. Paralysis of the hypoglossus was noted in five cases, and, of the abducens, in six. The accessorius was implicated in four cases, the oculomotorius in three, the trigeminal in one, and the vagus in two.

During the Swedish epidemic of 1905, I collected the following figures:

| | Cranial Nerve Affections Associated with Spinal Nerve Affection. | Cranial Nerves Alone Affected. |
|---|---|---|
| VII | 12 | 14 |
| XII | 9 | 9 |
| Eyes | 5 | 3 |
| VI | 4 | 2 |
| III | 4 | 2 |
| IX–XI | 5 | 4 |
| V | 2 | — |
| II | 1 | — |
| | 42 | 34 |

As shown in this table 42 different paralyses occurred in 34 patients; the 34 affections of cranial nerves, alone, occurred in 22 patients (vide page 63); therefore, it is evident that in a number of patients paralysis of the cranial appears in combination with paralysis of the spinal nerves. Leegaard in 311 cases of paralysis twice found the facial alone implicated (0.64 per cent.) and thrice, facial combined with spinal paralysis; once ptosis appeared associated with an affection otherwise confined to the spinal cord. Ed. Müller observed no fewer than 13 facial and 3 unilateral abducens palsies among 100 cases, but he detected no implication of the other cranial nerves.

Zappert collected 25 instances of combined cerebral and spinal nerve affections out of about 290 cases. During the Austrian epidemic, cases occurred in which only the cranial nerves were attacked, but with reference to these Zappert gives no exact figures. Spieler gave a more detailed report upon 44 such cases from this epidemic. Cranial nerves were involved in twelve cases, the facial in eleven, hypoglossal in five, the oculomotor in two, and the vagus in two. Bulbar disturbances of speech occurred;

nystagmus appeared twice, and difference of the pupils four times, twice due to spinal cord lesions, for the oculopupillary symptom was present. Three of these cases were almost exclusively bulbar-pontine in type, one showed associated cerebellar ataxia, four had spinal cord symptoms, and three were of the encephalitic type.

Among the 752 cases of the New York epidemic, involvement of the cranial nerves is reported to have occurred as follows: Facial palsy 27 (14 right, 4 left side, bilateral 2, side not specified, 7); eyelids, 18; strabismus, 26; difficulty in swallowing, 18; and speech affection, 28.

The inconsistency of these statements arises partly because reports of epidemics mostly are the result of collective investigations, in which the primary data may be imperfect, and partly because in regard to cranial nerve involvement as to other particulars, the features of the disease vary in different epidemics. In 1887, during the Stockholm epidemic, the keen observation of Medin detected 8 instances of facial palsy among 44 or 45 cases, but in the 1895 epidemic only 1.

Inflammatory changes are the basis of the signs of affection of the bulb and brain stem. Clinically the alteration in the cranial nerve nuclei is the most evident change, yet according to the current nomenclature these cases must be regarded as polioencephalitis. We must, however, distinguish superior polioencephalitis from inferior polioencephalitis. In superior polioencephalitis we must further, I believe, differentiate two forms—the recognized Wernicke form and one which I suggest should be named the Medin form. These two forms differ not only in their etiology but also in their general course.

Wernicke's form arises principally from intoxications, the most usual of which is alcoholic. It is generally accompanied by mental changes which may culminate in delirium tremens, and it usually pursues an afebrile, sometimes a subnormal temperature course. Hemorrhage is the common morbid change found in this form.

Entirely different are the conditions in the Medin form. Here, in harmony with the infectious nature of Heine-Medin's disease, we find inflammatory changes in the brain stem. The disease is, moreover, febrile and usually shows none of the psychic disturbances peculiar to the Wernicke form. There are resem-

blances between the Wernicke and Medin forms, but there are also distinct differences. I am of opinion, however, that cases of Heine-Medin's disease have been published under erroneous designations. Still more certainly has this occurred with regard to the second principal division—acute inferior polioencephalitis. Several maladies are included here which have in common that they, although of different origin, are all due to infectious processes; that they are characterized by similar pathological changes; and that they further correspond from the point of view of symptomatology. One of these varieties is nothing more nor less than the bulbar type of Heine-Medin's disease. The etiology, therefore, is the key to the differential diagnosis. All cases of Heine-Medin's disease with bulbar localization are cases of acute inferior polioencephalitis, but all cases of acute inferior polioencephalitis are not cases of Heine-Medin's disease.

As Heine-Medin's disease, during an epidemic, may express itself as a facial palsy, we may accept that, in sporadic cases, the disease may assume the same guise. Hence, some facial palsies which have been attributed to lesions of the seventh nerve trunk may really be due to inflammatory changes in the seventh nerve nucleus.

Oppenheim has repeatedly observed an initial febrile stage of one to three days' duration in young children, in whom facial paralysis acutely developed. He raised the question whether these paralyses were or were not sometimes of pontine origin. I, myself, observed a sporadic case of facial palsy which in great probability was due to Heine-Medin's disease, for the little brother of the patient was attacked about the same time by an abortive type of Heine-Medin's disease.

4. *The Cerebral Encephalitic Type.*—Although Vizzioli had already established the relationship of spinal and of certain forms of cerebral paralysis in children, Strümpell was the first to give us a complete description of the cerebral type of Heine-Medin's disease, which he called "Acute Encephalitis in Children (polioencephalitis acuta)." Pierre Marie in France also recognized this symptom complex as a disease entity.

Strümpell describes the disease as follows: "After an initial stage, in which fever, vomiting and well marked convulsions occur, paralysis develops. It may be a hemiplegia, a monoplegia, or a

facial paralysis, but it has the usual characters of a cerebral paralysis. In a number of cases, signs of motor irritation persist. Many patients show symptoms of epilepsy through life. In some the epileptic convulsions are confined to the afflicted side, but more frequently they are generalized epileptic seizures. Athetosis, chiefly of the hands, follows more often than epilepsy. Disturbance of speech sometimes appears; more often, a diminution of intelligence and moral deterioration are observed."

This acute polioencephalitis must be deemed a special form of cerebral infantile paralysis. Just as in acute poliomyelitis, here, also, the distinguishing and specific character is the short febrile initial stage. Medin's observations and other facts seem to establish the accuracy of Strümpell's teaching. Several physicians, however, have pointed out that the great recent epidemics apparently afford no indubitable substantiation of Strümpell's views. I shall here briefly discuss the results which have supported Strümpell's doctrine and also the objections which have been urged against it.

I shall first consider the pathological findings. Foci of encephalitis have been detected in all the recent cases which have been examined (Redlich, Wickman, Harbitz and Scheel). It was contended that as these foci were always very small, and as they produced no symptoms during life, they could be regarded only as symptomatic of a widespread affection of the central nervous system. Such a contention is quite correct, for the patient dies showing the usual spino-bulbar symptoms long before more extended encephalitic processes have time to develop. Two cases of Harbitz and Scheel ran a different course and as they are of great importance I may perhaps be allowed more fully to refer to them.

1. The patient was a man, 39 years old; the disease began with headache, fever and excessive sweating. A few days later stiffness of the neck, vomiting, delirium and general convulsions followed; in four days a left-sided hypoglossal paresis, rigidity of the limbs, exaggerated patellar reflexes, and, later, twitching of the left forearm and of the fingers appeared; coma was replaced by death on the thirteenth day of the disease. On macroscopic examination of the organs after death, no change was visible except a marked inflammation and softening of the right temporal

lobe, which at the frontal pole and over the under surface was so soft as almost to be diffluent. The changes were most marked in the cortex, but penetrated 2–3 cm. into the white matter, and effaced completely the line of demarcation between the cortex and the white substance. The process extended to the Island of Reil, also, and its surface was likewise softened, but only to a depth of 2–3 mm. A similar softening 8–10 cm. in extent, and 2–3 mm. deep, spread in a sagittal plane, on the mesial surface of both hemispheres, corresponding to the gyri fornicati. Microscopical examination revealed an acute inflammatory infiltration at these sites, in the central ganglia, pons, medulla oblongata; and a precisely similar change was present in the gray matter of the anterior horns of the upper cervical segments, such as has been often observed in cases of Heine-Medin's disease. A pial infiltration was found elsewhere in the spinal cord.

2. In the other case, a child seven years old suddenly developed fever, vomiting, drowsiness, twitching in the left elbow, knee and hip joints and rigidity of the neck muscles. Death occurred in four days. In this case, an acute encephalitis of the left optic thalamus was found. Otherwise, even upon microscopical examination, no abnormal condition could be detected except a hyperemia most marked in the neighborhood of the aqueduct of Sylvius and of the cervical region of the cord.

These two cases were observed in Christiania during the Norwegian epidemic of 1905, but their relation to the epidemic was left undecided by Harbitz and Scheel, as only 13 cases of acute poliomyelitis occurred in the whole city. The similarity of the morbid changes in each, and in the first the coexistence of unmistakable evidence of poliomyelitis, although not absolute proof, yet convince me that both were cases of Heine-Medin's disease.

Macroscopical findings have also been collected in cases of longer duration. Lamy found besides poliomyelitic changes in the lumbar enlargement, four foci in the cortex of the left cerebral hemisphere; one was in the parietal lobe, the others in the frontal. Still more extensive destruction of brain substance was established by Rossi in a man, 34 years old, who since childhood had suffered from paraplegia; the right leg was spastic and the left flaccid. On post-mortem examination, Rossi found a patch of sclerosis in the anterior horn region of the lumbo-sacral cord;

and, in addition, a widespread, bilaterally symmetrical destruction of the brain, implicating particularly the frontal lobe, the inner surface of the paracentral lobule and the great part of the corpus callosum.

In view of these proofs of the occurrence of extensive cerebral lesions in Heine-Medin's disease, I think that objections based upon the smallness of such lesions in most recent cases are not quite tenable.

The etiological identity of acute poliomyelitis and of Strümpell's polioencephalitis is supported first by the fact that flaccid and spastic palsies may occur in one and the same patient; and, second, that occasionally an epidemiological connection may be proved between cases of poliomyelitis and of encephalitis.

Williams, Neurath, Calabrese, Negro, Oppenheim, Pierre Marie and Wickman have reported cases of combined flaccid and spastic paralysis. Although it may be argued that the spasticity was due to a lesion of the pyramidal tract in the spinal cord, the case just quoted from Rossi shows that it may also be due to a cerebral lesion. Still more convincing in my opinion are the facts concerning the occurrence of spasticity during epidemics. Möbius observed a sister and brother affected with fever and malaise which they developed almost simultaneously. The one had a flaccid paralysis, as a sequel; the other a spastic hemiplegia with choreic movements. During the epidemic in Stockholm, Medin saw three cases which presented an acute febrile onset, somnolence, twitching and paralysis of one side of the body, and spastic symptoms. In one case, athetotic, in another, choreic movements appeared. Twice a paralysis of the abducens was observed. Concerning a fourth case, Medin admitted he was uncertain if it were a meningitis or a polioencephalitis, but its subsequent course with its rapid improvement and complete recovery convinced him it was a polioencephalitis. It corresponded perhaps more to the meningitic type.

Several other cases of Medin showed symptoms indicative of a brain lesion. One case in which the etiological relationship to Heine-Medin's disease seems to me to be placed beyond doubt is especially interesting: A small boy was feverish and somnolent; his legs and arms became paralyzed; and five days later, apparently after the appearance of respiratory difficulty, he died. The

physician considered the case to be meningitis, until the patient's brother a few days later developed fever and pain in the back. In this second case, after some time, a paralysis of the lower branch of the seventh nerve appeared, and then disappeared; and the knee jerks markedly increased. A contracture in the thigh muscles could be demonstrated by passive movement. The gait was spastic, broad-based, and uncertain. On account of this last symptom, Medin recorded the case as an acute ataxia. But I believe that here also was a case of encephalitis.

Against Medin's cases one might protest—as has been done—that they were merely coincidences and had no etiological relation to the prevailing epidemic of poliomyelitis. Anyone experienced in the pathology of children knows, however, that cases such as those described by Medin are extremely rare; and, besides, the death in the one case was typical of acute poliomyelitis.

Further observations have been made by Buccelli upon the synchronous occurrence of encephalitis and poliomyelitis. He studied, in 1897, in a restricted locality in Genoa, a small epidemic of 17 cases. Some of the cases were of a cerebral, others of a spinal type. In one house, where several children were ill, one developed spinal and two cerebral infantile paralysis (cited from Starr). Buccelli collected the cases of polioencephalitis treated in the polyclinic at Genoa, and found that they had been most frequent during summer. But neither Neurath in the Vienna, nor J. Hoffmann in the Heidelberg epidemic, was able to establish this connection.

Aug. Hoffmann reported the simultaneous illness of two children, one of whom presented a flaccid paralysis; the other, a spastic hemiplegia with athetosis, ankle clonus and Babinski's sign.

If now we turn to the larger outbreaks, we have to admit that they afford only meager corroboration.

During the Swedish epidemic, among all the hundreds of cases which I personally examined, I observed no case of spastic hemiplegia. It is, however, quite possible that among those I did not examine spasticity occurred. The reports made to me by my colleagues, in many instances, dealt mainly with the localization of the paralysis, and omitted to mention the condition of the reflexes. Only once a spastic paralysis of the arm was observed. Quite a number of my colleagues, however, reported the occurrence of aphasia which invariably proved transient.

Leegaard reports only two cases of encephalitis.

No case of spastic hemiplegia was recorded from the American epidemic. In one family, however, one child was said to be attacked by the spinal, and another by the cerebral type, but no further information was given; and aphasia was reported only in one case.

Ed. Müller, who had an opportunity to examine over one hundred patients, believes that there undoubtedly is a clinical form of Heine-Medin's disease, which may be called cerebral infantile paralysis, but that it is very rare. In four of Müller's cases only spastic paralysis developed; and in two, a spastic was combined with a flaccid paralysis. Another case, which Müller thinks was a brain lesion, showed a right-sided spastic paresis of the extremities, with implication of the right side of the face.

During the Austrian epidemic, Zappert observed three cases probably of an encephalitic nature. In one of these, the remains of a right-sided hemiplegia and an atrophic paralysis of the left leg coexisted.

In another, according to the statement of the attending physician, "a severe, febrile, acute encephalitis with left-sided paralysis" ended in recovery, and the third showed clinically and pathologically a combination of encephalitis and poliomyelitis.

In spite of the meager data, Zappert is disinclined to deny the essential relationship of encephalitis to Heine-Medin's disease. Spieler records three cases of encephalitis among the 44 patients admitted to the Karolinen-Kinderspital. Another case observed during the Vienna epidemic, but not reported by Zappert, is recorded by Schlesinger as belonging to the encephalitic type of Heine-Medin's disease.

In the neighborhood of Hamburg, Nonne observed in four villages, in 1905, a small epidemic of 22 cases. In most of the cases the common type of poliomyelitis occurred. In a few, however, unusual symptoms appeared: Nonne observed in two adults a unilateral encephalitic paralysis; both recovered without residues.

Krause also observed one case of encephalitis during the 1909 epidemic in Westphalia.

The testimony of the great epidemics upon this point has obviously been very slight. But in judging these facts we must con-

sider, first, that most of the material has merely been gathered from general reports; and, second, that the disease from time to time and from place to place not inconsiderably varies.

The first circumstance implies the possibility of lack of completeness in the primary data. Often in cases of hemiplegia, no reference was made to the patellar reflex. And further, if a spastic hemiplegia occurred, it depended upon the knowledge and personal opinion of the attending physician whether it was included with the other cases of poliomyelitis, or considered as an independent disease. In the latter contingency, the case was probably omitted from the statistics. On the other hand, encephalitis in the initial stage often simulates meningitis and usually is then so diagnosed, for practitioners are better acquainted with the nature of meningitis than of encephalitis.

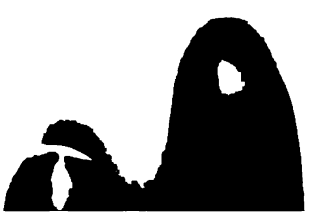
The second circumstance, the variability of the disease, must not be undervalued, but I have already dwelt upon it in the introduction.

The greatest difficulty seems to me to lie in the results of experimental poliomyelitis. In monkeys, after intracerebral injection, a poliomyelitis, not an encephalitis, regularly appears.

From all facts at our disposal, it is probable that in man the virus of Heine-Medin's disease may cause encephalitic changes. Symptoms may, therefore, arise in this disease of a very variable but distinctly encephalitic character. Occasionally, the encephalitic affection may assume the form of a hemiplegia, but this is rarer and of better prognosis than was formerly thought. Further exact observations are much needed on this subject.

Finally, I may mention Petrén's view that encephalitis is caused by a special virus, which occasionally gives rise to poliomyelitis. For lack of fundamental facts we shall not at present discuss this opinion.

5. *Ataxic Type.*—Medin observed during an epidemic of infantile paralysis that some cases showed only or chiefly ataxic symptoms. He compared these motor disturbances with those of Friedreich's ataxia. The child's walk is uncertain, staggering and wide-based. There is evident difficulty in maintaining balance: the child stumbles and falls often and readily. Medin's cases, however, showed symptoms which distinguished them from the typical spinal infantile paralysis: in none did atrophy of the



muscles develop; and in many the patellar reflexes were increased.

Wickman also observed instances in which ataxic symptoms were especially conspicuous. The ataxia was sometimes of a distinctly cerebellar type, but here paralysis of cranial, and, to a lesser degree, of spinal nerves also occurred. In other cases, the only demonstrable sign, besides the ataxia, was either diminution or loss of the patellar reflexes. These cases did not present the distinctive features of a cerebellar ataxia. Occasionally, the disturbances, although evident, were not prominent in the picture of the disease.

Ataxia was more frequently observed in subsequent epidemics. Its presence was mentioned by Zappert and Spieler in several cases in which it seemed to be associated with cranial nerve lesions. Lindner and Mally reported a case of cerebellar ataxia, paresis, and atrophy of the left thigh, marked increase of both patellar reflexes, and ankle clonus. The cranial nerves were not implicated.

A case of aphasia, paralysis of the right arm, and ataxia was described by Netter.

Nonne saw in a child during the Heidelberg epidemic a severe *status hemiepilepticus,* which was followed by a high degree of general ataxia of the acute cerebellar type. The case pursued a favorable course and ended in complete recovery.

The pathologic basis of the ataxia in my opinion is inconstant. Medin thought a neuritic process was concerned, but such seems hardly probable, for in all cases the tendon reflexes were increased. In cases which present cranial nerve signs, the ataxia may be due to an interruption in the coordinating tracts of the midbrain. Perhaps the ataxia may also arise from changes in the cerebellum, which have been found in almost every recent case examined. In other cases the lesion may be situated in the spinal cord—in Clarke's column, perhaps.

Zappert thinks it undesirable to consider ataxic cases separately. He prefers to include them with the bulbar, or pontine type. Although some undoubtedly belong to the bulbar type, there are many others in which the ataxia is not distinctly cerebellar in character, and in which all signs of either bulbar or pontine implication are absent. The fundamental site of the changes in these cases still evades us, but to imply for a whole group of cases certain changes which are perhaps not common to all, seems to me undesirable.

6. *The Polyneuritic Type.*—In the description of the initial symptoms, pain and general tenderness were mentioned as usual features of Heine-Medin's disease. If the pain be severe and be accompanied by tenderness on pressure over nerve trunks, we have a picture which corresponds completely with the disease described in all text books as peripheral neuritis. When these symptoms sporadically appear, a diagnosis of peripheral neuritis is made.

Medin first observed in an epidemic of infantile paralysis cases which resembled neuritis; and during the epidemic of 1905 I and numerous other Swedish physicians encountered similar cases.

The observations of later epidemics confirmed the occurrence of this form of the disease (Hartmann, Schlesinger, Foerster, Ed. Müller, V. Stark, Netter, Sachs and others). In all of Foerster's cases the nerve trunks in the limbs were hypersensitive, and tenderness was present on passive movements. Foerster found, also, in several patients the sciatic sign, which is mentioned by Wickman, Lindner and Mally. These cases may progress to recovery or remain permanently paralyzed. If recovery occurs, harmony with the text book description of acute neuritis becomes still more perfect. Rarely, disturbances of sensibility appear. Close examination has shown that these sensory disturbances have a dissociated character. Obviously, this fact can hardly be demonstrated in little children, in whom sensory examinations are perforce restricted exclusively to the pain sense.

It is still undecided if these clinically polyneuritic forms really arise from inflammatory changes in the nerves. I personally am of opinion that they are exclusively produced by central changes and therefore it would, from my point of view, be more correct to designate them pseudo-neuritic. But post-mortem examination in Heine-Medin's disease has never revealed the presence of neuritis. Objective disturbances of sensibility are usually lacking; and it is difficult to reconcile in such cases the existence of a widespread paralysis and a lack of objective sensory disturbances upon the basis of a neuritis.

Indeed, microscopical examinations of fatal cases of Heine-Medin's disease have not yet disclosed any changes in the peripheral nerves. But on the other hand, such examinations have been restricted in extent and few in number; and so far as I know

have not been made upon cases which from the distinctness of the neuritic symptoms definitely belong to this group. Although we can, therefore, say that the existence of a neuritis in Heine-Medin's disease has not been histologically demonstrated, we cannot completely exclude its possibility.

It is, however, quite certain that Heine-Medin's disease is frequently indistinguishable from spontaneous, infective, acute polyneuritis and it cannot be differentiated from the "amyotrophic plexus, neuritis of infancy," described by E. Remak. As in each of these, the paralysis directly follows a febrile initial stage, both stand, in all probability, in direct etiological relation to Heine-Medin's disease. I think it is of practical importance to distinguish a neuritic or pseudo-neuritic type of Heine-Medin's disease.

7. *The Meningitic Type.*—The signs of meningeal irritation, which can often be observed in Heine-Medin's disease, may, under certain conditions, attain such prominence as convincingly to resemble some form of meningitis. Vomiting, headache, pain and rigidity in the neck and back, opisthotonus, Kernig's sign, tonic and clonic spasms, strabismus, coma, etc.—all the symptoms of an acute meningitis in all degrees and in all possible combinations may be added to the picture of the disease. Only in the chronic stage does the course differ from that of a meningitis. In most cases, the signs of irritation cease and the characteristic palsies of Heine-Medin's disease become evident. In some, the disease, even after it has assumed a most threatening aspect, disappears in a tolerably short time and an astoundingly complete recovery ensues. In others, under a more or less stormy aspect, the malady runs a lethal course.

During the Swedish epidemic, numerous transitions from distinct meningitis to typical poliomyelitis were observed. Upon this clinical basis and upon the epidemic connection of these meningitic cases with proven poliomyelitis, Wickman established a special meningitic form of Heine-Medin's disease. The following are two typical examples of this meningitic form:

The first developed convulsions, marked somnolence, stiffness of the neck, opisthotonus, hyperesthesia, persistent tonic spasm of the limbs, strabismus, inequality of the pupils and retention, with subsequent incontinence, of urine. All these symptoms disappeared within two weeks and left no trace.

The second, an adult, had fever, headache, vomiting, pain and stiffness in the neck and tonic spasms in some of the muscles of the shoulders and arms. Later, cramps in the legs appeared; then, opisthotonus; and, finally, difficulty in speech and in swallowing developed and death came three days after the illness began. As this patient was pregnant, the physician thought she suffered from eclampsia. He therefore induced premature labor. Post-mortem examination showed in the spinal cord the changes typical of acute poliomyelitis. In connection with this case, some others of a transient nature are mentioned on page 77. Upon epidemic, clinical and pathological grounds, the meningitic type is in established relation to Heine-Medin's disease. This has been confirmed by others. Leegaard in his statistics of the Norwegian epidemic reports cases which he enumerates as cerebrospinal meningitis, but which undoubtedly belong to this group. Zappert states that according to his observations during the Austrian epidemic the existence of this type is beyond doubt. Spieler's statements about similar cases are of such great interest that I shall here quote them literally: In 8 out of 44 cases of Heine-Medin's disease, admitted to the Karolinen-Kinderspital in Vienna, more or less pronounced and typical meningeal symptoms were present. The picture of the disease in four of these eight so resembled a tuberculous meningitis that not until some time had elapsed was its relation to Heine-Medin's disease suspected. For a week or more the well known prodromal symptoms—change in disposition, tiredness, nocturnal restlessness, screaming, occasional vomiting and obstipation—suggestive of commencing basic meningitis were present. This suggestion was reinforced by the sudden appearance of convulsions, which were associated with marked rigidity of the neck, irregularity of the pulse, Kernig's sign, transitory increase of the patellar reflexes, strabismus, general cutaneous hyperesthesia, vasomotor disturbances, and typical cerebral facies. The deception was still further enhanced, for lumbar puncture yielded a clear fluid which was under increased pressure, which formed a distinct diffuse, non-reticular, fibrinous clot; and which, on cytological examination, showed only numerous lymphocytes. At length, the noteworthy retrogression of the signs of irritation, and, later, of the cranial nerve symptoms; the complete disappearance of the fever; the more or less localized, flaccid

paralysis of limb, of abdominal, and—as occurred in a private case—of isolated neck muscles, together with the appearance in them of the reaction of degeneration, and recovery either complete or associated with permanent, more or less diffuse, flaccid paralysis and atrophy of the muscles, permitted no doubt that these were cases of Heine-Medin's disease.

In the epidemic in New York, a case occurred in which convulsions, rigidity of the neck, Babinski's sign and Kernig's sign led a distinguished pediatrist to diagnose meningitis (Schwartz). Hochhaus saw two cases in which post-mortem examination demonstrated conclusively Heine-Medin's disease, although the clinical course had been that of an acute meningitis. Netter called attention to the striking and frequent occurrence of signs of meningeal irritation during the Paris epidemic of Heine-Medin's disease. Kernig's sign was very often noted. One child was sent to the hospital with a diagnosis of cerebrospinal meningitis. Netter observed one case in which the spinal fluid was somewhat cloudy and yielded a fine cobweblike coagulum; but in another, the fluid was clear. Netter further noted that in one third of his cases the disease began with distinct meningeal symptoms. He was able to prove in Paris, synchronous with the epidemic of poliomyelitis, the prevalence of a benign form of meningitis which he considered—correctly, I believe—to belong to the meningitic type of Heine-Medin's disease.

Occasionally the spinal fluid coagulates (Netter and Spieler). Its other characters have already been discussed in dealing with the acute stages (page 29).

How closely Heine-Medin's disease may resemble ordinary meiningitis has just been narrated. The knowledge of this meningitic form helps us to explain the statements of observers such as Caverley and Macphail, and Mackenzie, who reported that cerebrospinal meningitis and poliomyelitis may occur simultaneously. It also bares the foundation of the belief that these two diseases are related. Wickman proved that where exact data were available no such relationship existed and he suggested that in both of the recent American outbreaks numerous and definite cases of the meningitic form of Heine-Medin's disease, alone, occurred.

*The Abortive Form.*—During the Swedish epidemic of 1905,

in the immediate neighborhood of well-defined cases of poliomyelitis, and in distinct etiological connection with them, many patients were discovered who showed only general symptoms of being ill and presented no signs of paralysis. Such cases Wickman designated *Abortive Cases*. Between the definitely abortive case running a course characterized merely by malaise, or by slight and fleeting palsies, and the completely typical and, even, sometimes, fatal case, the existence of transitional forms was clearly established. Indeed, these various forms were occasionally exemplified among the respective members of one family.

The picture of the abortive type corresponds in general with that of the initial stage of typical infantile paralysis. The attack as a rule is acute and accompanied by fever, headache and general malaise. In some cases these symptoms are associated with others, such as rigidity of the neck; pain in the neck, back, loins, and limbs; and paresthesia; which point to implication of the nervous system. But these symptoms are not followed by paralysis. The patient usually recovers within several days and no trace of the disease remains except prostration which may be protracted. The abortive case thus presents only symptoms of a general infection and no real localizing signs. Even if the disease sets in suddenly, vague, ill-defined prodromal symptoms, such as exhaustion, mark its commencement. But after a few days generally the symptoms become acute. In discussing the initial stage it was mentioned that the height of the fever and the severity of the other signs are not significant of the further course of the disease. In abortive cases simultaneous with the usual complaint of headache is that of pain in the neck. Rigidity of the neck muscles is often then detected. In the abortive case not infrequently symptoms perhaps attributable to meningeal irritation arise. More or less marked opisthotonus even may occur. The disease then closely resembles meningism. Such cases are a link with the definite meningitic type of the disease. Among other signs of irritation pain in the limbs is especially marked. Usually several extremities are tender but sometimes only one. Sometimes the severity of this tenderness is extreme. In such cases, for want of a better, a diagnosis of influenza is often made.

Nausea, vomiting, diarrhea and other gastrointestinal symptoms have frequently been observed in association with the abortive

type; sometimes so marked were they that gastrointestinal catarrh was suspected.

Wickman distinguishes the following varieties of the abortive type:

1. Cases running the course of a general infection.

2. Cases in which signs of meningeal irritation are especially prominent ("pseudo-meningism").

3. Cases accompanied by distinct tenderness ("pseudo-influenzal").

4. Cases with gastrointestinal disturbances.

Sometimes cases belong exclusively to one, more often to several of these varieties. As cases in which weakness or paralysis of the extremities or of the cranial nerves appears and quickly disappears might also be included among the abortive, this form obviously cannot be sharply differentiated from the others. These transient palsy cases Ed. Müller calls "rudimentary"; those I have described as "abortive" he calls "masked." As an example of how gradual the transition between the various forms may be, Wickman relates an indubitable case in which the only objective sign was diminution of one patellar reflex. On the other hand, Wickman also observed abortive cases in which the patellar reflexes were increased. Leegaard in his report of the Norwegian epidemic estimated that more than one third of all his cases were of the abortive type. Similar cases, although rarely reported, occurred in subsequent epidemics. The reasons for the rarity of reported abortive cases are, first, that reports are based upon collective investigations, the primary data for which are furnished only after the acute stage has passed; and, second, that physicians as a rule are unaware that such symptoms belong to Heine-Medin's disease. Yet the existence of the abortive type can be proved in these epidemics. Records of the New York epidemic mention that cases with symptoms of a severe general infection with or without temporary paralysis were observed by various physicians. Zappert definitely states that, within small infected localities, he was able to establish the occurrence of a number of cases of obscure fever synchronous with the appearance of poliomyelitis. Physicians remarked frequently upon the cases of "influenza" and upon the gastrointestinal symptoms which developed in the vicinity of the cases of poliomyelitis. Zappert reports further a small

localized epidemic in which about 20 persons were attacked by symptoms resembling influenza; in 10 of these people developed characteristic paralysis; no paralysis appeared in the others.

Ed. Müller particularly studied the abortive forms in the epidemic in Hesse-Nassau. He verified the varieties I described, and, in addition, found cases evolving as bronchitis, or as sore throat. He, also, observed the connection between the several varieties. For instance, he saw one family in which three children were attacked with gastrointestinal symptoms. In the first child the symptoms all disappeared; in the second, only loss of tendon reflexes persisted; while in the third, typical paralysis ensued.

Krause, who noted many cases of the gastrointestinal variety, mentioned that often the other members of the family suffered from diarrhea. "In one family," he reports, "seven persons were thus attacked."

Records of abortive cases have accumulated recently, especially from the American epidemic (Lovett, Armstrong Davis, Ball and others).

It may, therefore, be safely asserted that the occurrence of abortive forms during epidemics is a regular phenomenon.

Abortive cases represent a considerable proportion of all the cases in any epidemic. Their exact ratio we cannot yet determine. Wickman's statistics of the Swedish epidemic of 1905 contain 968 paralytic and 157 abortive cases. But as the abortive cases could be accurately enumerated only in limited districts, their total is underestimated here. In the several areas carefully examined, the proportion was quite inconstant. In one epidemic center, of 31 cases, 11 (35 per cent.) were abortive. In another, where every case was detected, 49 cases were observed, of which 23 (46 per cent.) were abortive. In yet another, which was studied by Wickman, 56 per cent. were abortive. It is not impossible that the frequency of those abortive cases, under certain conditions, may be even greater.

A large number of abortive cases have been observed and described by Brorström, who believes that they are more frequent than the paralytic cases. He considers, however, acute poliomyelitis as a variety of influenza and admits, therefore, many cases which have no claim to discussion here.

Leegaard, among 952 cases, found 358 of the abortive type. He remarks that this figure is too low; that such cases are to a great extent overlooked, and that, without exaggeration, the abortive forms might be estimated at about one half of the total cases.

Ed. Müller is of the opinion that the abortive are far more numerous than the typical cases, especially among adults. Müller thinks it possible that the abortion of the disease is due to an acquired immunity. I can neither confirm nor deny Müller's statements, but, at least, within the foci I studied a relatively greater frequency of the abortive type in adults was not evident. If acquired immunity had any practical importance in this question some great epidemics must be presumed to have occurred and to have conferred protection on the large number of people who now enjoy it. But epidemics of former years are unheard of in Germany. Müller's hypothesis, however, is highly interesting, and will be more accessible to examination when serological methods of investigation are simplified.

The common origin of the abortive and paralytic forms was established by clinical and epidemiological observations in Sweden. Further evidence of this etiological identity has lately been obtained by Levaditi and Netter. In the blood of a girl who was attacked by an abortive variety of Heine-Medin's disease, and who developed no paralytic symptoms, these observers found substances exercising a specific neutralizing action upon the poliomyelitis virus. This child's brother was attacked at the same time by typical infantile paralysis and similar antibodies were found in his blood.

Finally, in the experimental poliomyelitis of monkeys, also, abortive varieties have been observed.

The abortive type is of great importance, especially as regards the epidemic behavior of the malady. Obviously, the spread of the disease presents a totally different aspect if we consider not only the typical but also the abortive cases.

## CHAPTER VI

### Diagnosis and Differential Diagnosis

As a general rule, a diagnosis of Heine-Medin's disease is justifiable if, after a short, acute, febrile, initial stage, paralysis of flaccid type develops. The paralysis attacks usually the leg, trunk or arm muscles; rarely, the muscles supplied by the cranial nerves. During the initial stage, symptoms such as general tenderness, rigidity of the neck, sweating and somnolence are to a certain extent characteristic.

As Heine-Medin's disease often presents at the onset only the general characters of an ordinary infectious disease, we must be prepared to distinguish it from similar conditions due to other infections. If well-marked general tenderness be present a suspicion either of influenza or of a rheumatic affection may arise. The latter, as a rule, is easily excluded; the tenderness in rheumatic affections is usually localized to joints; whereas, in Heine-Medin's disease such a localization, although it may occur and be associated even with joint swelling, is extremely rare.

To differentiate from influenza is more difficult. Clinically influenza has become as a lumber room in which most heterogeneous conditions are lodged. Heine-Medin's disease may be separated from a real influenza produced by Pfeiffer's bacillus: in Heine-Medin's disease catarrhal symptoms, although generally present, are less, whereas sensory irritability as a rule is more severe than in influenza. Yet, a bronchitis, a conjunctivitis, or other catarrhal inflammation may appear in the course of infantile paralysis.

If gastrointestinal symptoms are present, or if they predominate, an intestinal catarrh may be suspected. But in such cases, usually, some symptom, such as tenderness, or sweating, suggests that the nervous system is implicated.

What has just been said applies to the abortive forms. These can be diagnosed with certainty only if they appear during an epidemic, or if they are associated with cases either of paralysis, or of indubitable implication of the nervous system. Among the

most important of the signs of involvement of the nervous system is alteration of the reflexes. The alteration may consist either of an increase or of a decrease. Hypotonus without actual paralysis has been described occasionally. Any unilateral alteration of the reflexes must be regarded as abnormal. We have to guard, however, against concluding too hastily that the reflexes are absent, especially in children in whom, owing to muscular tension, deep reflexes are often difficult to elicit.

In the initial stage, marked and occasionally persistent meningeal symptoms may easily be mistaken either for epidemic cerebrospinal or for tuberculous meningitis. But Heine-Medin's disease very rarely presents a herpes labialis such as so often occurs in cerebrospinal meningitis; and psychic disturbances are more marked usually in cerebrospinal meningitis. Petrén is of the opinion that the tendency to an exclusive spinal localization of the meningitic symptoms in Heine-Medin's disease differentiates it from cerebrospinal meningitis; but although cerebral symptoms do predominate in cerebrospinal meningitis, yet each of these diseases has shown such great variation in this respect that selective localization, even when well defined, may mislead. The most reliable means of discriminating lies in the use of lumbar puncture. In cerebrospinal meningitis, the cerebrospinal fluid appears cloudy; presents a leucocytosis; and may contain the intracellular meningococci.

In tuberculous meningitis, and in Heine-Medin's disease, lumbar puncture yields no such distinctive features; in both the fluid is clear, shows lymphocytosis, and coagulates; but in tuberculous meningitis the clot forms a characteristic central thread. The rapidity of onset of each disease is very variable but tuberculous meningitis tends to develop more slowly. Indeed, as was shown in Spieler's description, the similarity of these two conditions may be extraordinary. The diagnostic difficulty is especially great in the pure meningitic types, but if tubercle bacilli can be demonstrated, or if characteristic palsies appear, the nature of the case becomes at once apparent.

The existence of motor disturbances is by no means always so evident as to be obvious immediately. Sometimes, in the beginning of the disease, careful search is necessary. Especially in little children, repeated and skilful observation may be needful to

establish the precise nature of the disturbance. In older children and in adults the diagnosis of paralysis is easier. If paralysis be demonstrable, then we have its character and the anamnesis to enable us to decide whether the disease is or is not Heine-Medin's. If it is, we shall learn that the patient became suddenly ill with the well-known initial symptoms. But we must bear in mind that painstaking investigation is sometimes necessary in order precisely to ascertain the history of the development of the illness; and further, that the initial symptoms may, although rarely, be vague.

The differential diagnosis from multiple neuritis is of some importance. A sharp distinction has here to be made between the various forms of neuritis—the toxic, the infective, and the post-infective. Of the toxic forms of neuritis the most common are those due to alcohol, arsenic and lead. The paralysis which appears in any one of these, as a rule, is symmetrical; diminishes in severity centripetally; and develops much slower than, and lacks the febrile initial stage of, Heine-Medin's disease. The exciting causes can generally be ascertained in alcoholic neuritis and lead palsy. Both of these, in consequence of their special etiology, occur exclusively in adults.

Among the post-infective forms of neuritis, diphtheritic polyneuritis in children may closely resemble Heine-Medin's disease. The resemblance may be so great—especially if no history be obtainable and the paralysis be extensive—that, at first, it may be practically impossible to differentiate between them; moreover, Heine-Medin's disease may begin with sore throat. In the last case, however, paralysis develops immediately when the throat affection occurs and not, as in diphtheritic palsy, some time afterwards. Diphtheritic palsy almost invariably affects the soft palate and the muscles of accommodation. Patients suffering from diffuse diphtheritic palsy look cachectic and often have a tolerably characteristic grayish yellow complexion. Symptoms, such as irregularity of the heart's action and cardiac dilatation, may be present in diphtheria but not in Heine-Medin's disease. One of the most important distinguishing features is the gradual development of diphtheritic palsies. If a recent case present combined bulbar and spinal symptoms—a picture common in diphtheritic paralysis and possible in Heine-Medin's disease—and if the history of the

development of the affection be vague and meager, the disease is probably Heine-Medin's. The symptoms of Heine-Medin's disease may reach their maximum in a sick, recumbent child so rapidly as to escape the notice of the child's parents; whereas, in diphtheria the motor disturbances are noted usually before they become so widespread as to give rise to the suspicion of Heine-Medin's disease.

Epidemics have taught us that the clinical entity known as infective neuritis may be produced by the virus of acute poliomyelitis, that there is a neuritic type of Heine-Medin's disease. I believe we cannot differentiate this type of Heine-Medin's disease from many of the cases of so-called idiopathic infective polyneuritis. No distinction exists between them; they are identical conditions. If in immediate relation to a short febrile stage, paralysis suddenly develops, and if no sensory disturbances exist except spontaneous pain and tenderness on pressure especially over nerves, Heine-Medin's disease is probably present. No other virus, apart from that of rabies, is known to attack the nervous system in such a fundamentally specific manner as the virus of Heine-Medin's disease. The existence of sensory disturbances has been looked upon as a distinguishing feature between acute polyneuritis and the spinal form of acute poliomyelitis. But sensory changes are not constant in the former and they have been observed in the latter disease. When sensory loss, however, does occur in Heine-Medin's disease, it is not marked; it is seldom persistent; and it affects only the sensations of pain, heat and cold. These sensory changes arise from implication of the posterior horn. They can be satisfactorily demonstrated only in adults. In children, as dissociated sensory loss is difficult to determine, the disturbance is usually charted as a complete anesthesia. But if decreased perception of all forms of sensation really exist, or if the sense of touch be diminished and tenderness on pressure be present, the case is one of neuritis. If a neuritis be encountered its exciting cause remains to be discovered. It may be produced by the virus of Heine-Medin's disease or by other infective agents. Pathological investigation, mainly because of the limited extent to which recourse has been had to it, has not yet yielded any means by which we may differentiate these various infective agents. I think it necessary to separate the pathologic from the etiologic

aspect until their relationship be made clear by our own experience in epidemics. No text book, as yet, advocates my attitude on this point. Contrary to custom, I hold that the outcome of the disease ought not to determine the diagnosis; and a recovery from paralysis should indicate *in dubio* a polyneuritis. In a number of cases of poliomyelitis also recovery assuredly occurs. The most that may be said is that the persistence of paralysis is presumptive evidence of poliomyelitis; whereas, a benign course may equally indicate either a polyneuritis or a poliomyelitis.

The occurrence of dissociated disturbance of sensibility, combined with flaccid paralysis—to which reference has just been made—raises the question of the differential diagnosis from syringomyelia, but the essentially chronic course of syringomyelia at once distinguishes it from Heine-Medin's disease. Rarely, a case of hematomyelia presents the clinical aspect of acute poliomyelitis; but striking disturbances of sensibility usually exist in the former, together with a history of a trauma, and of an afebrile development.

Other varieties of myelitis, such as syphilitic myelitis, compression myelitis, and caisson paralysis, vary in symptomatology according to the localization of the disease focus. They chiefly differ from acute poliomyelitis in their sensory changes in which usually all forms of sensation are implicated. In addition, bladder trouble is commonly conspicuous in these varieties and their clinical picture is that of a transverse myelitis. Rarely, syphilis, principally through vascular changes, causes a paralysis which in distribution and in other respects corresponds to that arising from an acute poliomyelitis. From cases of such paralysis we must distinguish instances of Heine-Medin's disease occurring in luetic subjects and evolving in the customary manner.

A closer resemblance exists between labor paralysis, myatonia congenita, and Heine-Medin's disease.

In labor palsies the deciding factor is again the anamnesis. Heine-Medin's disease may assume the characteristic localization of a plexus paralysis. If no history be obtainable, a differential diagnosis may be almost impossible, especially when the paralysis has persisted for years.

In myatonia congenita (Oppenheim) great weakness with flaccidity of the muscles and joints rather than actual paralysis is

present. Myatonia congenita extensively implicates the extremities, is congenital, and seems usually to be degenerative.

In the suddenly developing pseudo-paralysis of rickets only extreme feebleness of the limbs is evident; the electrical reactions remain unimpaired. But according to Oppenheim atrophy may occur here, also.

In older children and in adults the question of hysteria arises sometimes. In hysteria sensory changes occur often; the reactions are normal, and atrophy is absent.

Hip disease may simulate paralysis but examination will readily enable the one to be distinguished from the other.

The so-called paralysis of Parrot which occurs occasionally in congenital syphilis must also be mentioned here. It is not a paralysis; the immobility in this affection is maintained because of the painfulness of the diseased bones; the electrical reactions are normal; the condition usually appears during the first weeks of life and other symptoms of inherited lues, such as "snuffles" or eruptions, etc., are present also.

Progressive muscular atrophy may be confounded with the chronic stage of Heine-Medin's disease, but, whereas the latter remains stationary, progressive muscular atrophy and poliomyelitis chronica advance. Difficulties in diagnosis ought therefore to arise here only if all information concerning the onset and course of the disease be denied. It has already been mentioned that progressive muscular atrophy attacks occasionally a person previously afflicted by infantile paralysis.

Heine-Medin's disease may run a course resembling Landry's paralysis. I am of the opinion that a clinical differentiation of these conditions is impossible at present.

In the accepted nomenclature the bulbar and pontine types of Heine-Medin's disease may be designated, according to the site of the lesion, acute superior, or acute inferior polioencephalitis. It has already been remarked that we have at least two types of acute superior polioencephalitis, Wernicke's and that which I have named Medin's type. Further research is required to determine if still others exist.

Wernicke's type is characterized by very well defined psychic symptoms, profound alterations in consciousness, delirium tremens, etc., and by an afebrile onset; the ocular muscles are usually para-

lyzed symmetrically or in groups. The history discloses an etiology in which intoxication, especially from alcohol, plays an important part.

Medin's type, in contradistinction, shows the febrile onset, characteristic of an acute infectious disease. Psychic symptoms are, as a rule, absent; and when they are present they usually consist of drowsiness and not of delirium. Rarely is the distribution of the ocular palsies symmetrical; frequently it is very irregular.

The bulbar type of Heine-Medin's disease may sometimes be differentiated by means of the history from acute inferior polioencephalitis. But further investigation undoubtedly is necessary in order definitely to separate these conditions.

Special reference must be made to the occurrence of facial palsy in Heine-Medin's disease. When such a palsy appears sporadically it is invariably considered as a peripheral paralysis. Clinically to differentiate a facial nerve palsy from a facial nucleus palsy due to Heine-Medin's disease in many cases is scarcely possible. Usually the former is more marked than the latter, but the febrile stage of the latter is the only practical distinction. It is perhaps unnecessary to state that in children the first step in the diagnosis of a facial palsy is to exclude the most common of its causes—middle ear-disease.

Loss of reflexes, atrophy, and electrical changes distinguish the hemiplegic type of spinal infantile paralysis from a cerebral infantile paralysis. The encephalitic variety of Heine-Medin's disease when it assumes a hemiplegic form is distinguished by its febrile onset from other forms of cerebral paralysis in children.

## CHAPTER VII

### Prognosis

When we speak of the prognosis of Heine-Medin's disease we must, more than in most other diseases, distinguish between the prognosis *quoad vitam* and the prognosis *quoad valetudinem completam*. That infantile paralysis never or hardly ever ran a fatal course, and that permanent paralysis always ensued, had formerly the weight of a dogma. Medin and Rissler proved that infantile paralysis could end fatally. Wickman later showed that, under certain conditions, the prognosis quoad vitam ought to be guarded; that a high mortality might prevail; and that the disease was more fatal to adults than to children. The Swedish epidemic of 1905 demonstrated further that the prognosis quoad valetudinem completam is more favorable than was credited formerly.

The mortality fluctuates considerably, not only in different centers of the same epidemic, but even at the various points of a single center. In one small epidemic area of 26 cases, Wickman found a mortality of 42.3 per cent.; in another, of 41 cases, the death rate was only 10 per cent.

The general aspect of an epidemic varies materially according as the abortive cases are estimated or not; and even when they are estimated, it changes according to the thoroughness with which the estimation is made.

The following table shows the figures accessible to me from European epidemics.

I reported altogether 1,025 cases with 125 deaths; 868 cases showed paralysis; 157 were abortive. For the sake of comparison with other epidemics and because the actual number of abortive cases was far in excess of those I reported, I have calculated the mortality with reference only to the 868 cases of paralysis. I have omitted the deaths which occurred after two weeks, for then the fatal termination always arose from a complication such as pneumonia developing in consequence of the paralysis. Fourteen deaths were thus excluded; one hundred and forty-five remained and are inserted in the table.

lyzed symmetrically or in groups. The history discloses an etiology in which intoxication, especially from alcohol, plays an important part.

Medin's type, in contradistinction, shows the febrile onset, characteristic of an acute infectious disease. Psychic symptoms are, as a rule, absent; and when they are present they usually consist of drowsiness and not of delirium. Rarely is the distribution of the ocular palsies symmetrical; frequently it is very irregular.

The bulbar type of Heine-Medin's disease may sometimes be differentiated by means of the history from acute inferior polioencephalitis. But further investigation undoubtedly is necessary in order definitely to separate these conditions.

Special reference must be made to the occurrence of facial palsy in Heine-Medin's disease. When such a palsy appears sporadically it is invariably considered as a peripheral paralysis. Clinically to differentiate a facial nerve palsy from a facial nucleus palsy due to Heine-Medin's disease in many cases is scarcely possible. Usually the former is more marked than the latter, but the febrile stage of the latter is the only practical distinction. It is perhaps unnecessary to state that in children the first step in the diagnosis of a facial palsy is to exclude the most common of its causes—middle ear-disease.

Loss of reflexes, atrophy, and electrical changes distinguish the hemiplegic type of spinal infantile paralysis from a cerebral infantile paralysis. The encephalitic variety of Heine-Medin's disease when it assumes a hemiplegic form is distinguished by its febrile onset from other forms of cerebral paralysis in children.

## CHAPTER VII

### Prognosis

When we speak of the prognosis of Heine-Medin's disease we must, more than in most other diseases, distinguish between the prognosis *quoad vitam* and the prognosis *quoad valetudinem completam*. That infantile paralysis never or hardly ever ran a fatal course, and that permanent paralysis always ensued, had formerly the weight of a dogma. Medin and Rissler proved that infantile paralysis could end fatally. Wickman later showed that, under certain conditions, the prognosis quoad vitam ought to be guarded; that a high mortality might prevail; and that the disease was more fatal to adults than to children. The Swedish epidemic of 1905 demonstrated further that the prognosis quoad valetudinem completam is more favorable than was credited formerly.

The mortality fluctuates considerably, not only in different centers of the same epidemic, but even at the various points of a single center. In one small epidemic area of 26 cases, Wickman found a mortality of 42.3 per cent.; in another, of 41 cases, the death rate was only 10 per cent.

The general aspect of an epidemic varies materially according as the abortive cases are estimated or not; and even when they are estimated, it changes according to the thoroughness with which the estimation is made.

The following table shows the figures accessible to me from European epidemics.

I reported altogether 1,025 cases with 125 deaths; 868 cases showed paralysis; 157 were abortive. For the sake of comparison with other epidemics and because the actual number of abortive cases was far in excess of those I reported, I have calculated the mortality with reference only to the 868 cases of paralysis. I have omitted the deaths which occurred after two weeks, for then the fatal termination always arose from a complication such as pneumonia developing in consequence of the paralysis. Fourteen deaths were thus excluded; one hundred and forty-five remained and are inserted in the table.

| | | Total of Paralytic Cases | Total Deaths | Mortality, Per Cent. |
|---|---|---|---|---|
| Wickman | Sweden, 1905 | 868 | 145 | 16.7 |
| Leegaard | Norway, 1905 | 577 | 84 | 14.56 |
| Zappert | N. Austria, 1908 | 266 | 29 | 10.8 |
| Lindner and Mally | E. Austria, 1908 | 71 | 16 | 22.5 |
| Fürntratt | Styria, 1908 | 433 | 57 | 13.16 |
| Krause | Germany, 1909 (Arnsberg) | 633 | 78 | 12.3 |
| Ed. Müller | Germany, 1909 (Hesse-Nassau) | 100 | 16 | 16 |
| Peiper | Germany, 1909 (Pomerania) | 51 | 6 | 11.7 |
| Eichelberg | Germany, 1909 (Hanover) | 34 | 7 | 20.55 |

These figures of the table show incontestably that during the epidemic in Europe a fairly heavy mortality prevailed. The mortality of the American epidemics was lower. In the New York epidemic the case mortality was estimated to be 5 per cent.; in 1907 Lovett reported a mortality of 4.7 in Massachusetts; of 234 cases 11 died. In 1908 he collected, in the same part of the State, 136 cases, but their mortality was only 2.94 per cent. Emerson recorded a synchronously occurring epidemic (1908) in another part of Massachusetts in which the mortality was as high as 7.24 per cent.

The death rate is much greater in adults than in children. In Wickman's report the mortality from birth to 11 years (592 cases of paralysis, 71 deaths) was 11.9 per cent.; whereas, between the age of 12 to 32 years (250 cases of paralysis, 69 deaths) it rose to 27.6 per cent. The statistics of Leegaard show this same ratio, although the fact seems to have escaped his attention. If Leegaard's figures be calculated in percentages, they show from birth to 14 years a mortality of 12.4 per cent. (404 cases of paralysis, 50 deaths); but between 15 and 30 years a mortality of 25 per cent. (132 cases, 34 deaths). If a similar reckoning be made with the figures from Fürntratt's table we find a mortality of 11.05 per cent. in the age period from 0–14 years (407 cases, 45 deaths); but a mortality of 25.53 per cent. above 15 years (43 cases, 11 deaths). Still more striking are the figures of Mally and Lindner: Between 0 and 11 years, 59 cases of paralysis of which 10 were fatal; *i. e.*, a mortality of 16.9 per cent.; above 11 years, 12 cases of paralysis, of which 6 were fatal; *i. e.*, a mortality of 50 per

cent. These several statistics are obviously in harmony on this point and those from the other epidemics are not in discord. The figures for adults are admittedly too few to permit of any positive conclusion. But as the sum of the cases observed by Wickman and Leegaard is exceptionally large (1,378 cases of paralysis, 224 deaths), and as their cases were collected under very similar conditions, the greater mortality in adults and older children which their statistics show may be taken as an established fact.

With respect to the danger upon different days of the disease, there is no uniformity. According to Wickman, life is in greatest peril between the third and seventh days, and the fourth is the most fatal day. Leegaard's figures show that death occurred most frequently on the third or fourth day. Ed. Müller affirms further that on the fourth day severe paralysis most often appears. After the lapse of the second or third week, in cases in which the function of the respiratory muscles is seriously impaired by paralysis, life is especially menaced by pneumonia.

We have next to consider, in the prognosis, the patient's prospect either of escaping wholly, or of recovering completely, from paralysis.

In the discussion of the symptomatology we mentioned that many cases recover rapidly, without ever presenting symptoms of paralysis. But as the frequency of these cases seems considerably to vary, just how great is their proportion cannot be decided at present. Nor can we yet determine the influence of age upon this aspect of the prognosis for our available data are still too meager. Of my 699 patients between the ages of 0 and 11 years, 107—15.3 per cent.—were abortive cases; whereas, of my 299, between the ages of 12 and 32 years, 49—16.4 per cent.—were abortive. Among Leegaard's 615 cases under 15 years of age, 34.31 per cent. (211) were abortive; and of the 179 above 15 years, 26 per cent. (47), were abortive. We cannot extract a generalization from these figures, as the census of the abortive cases was not sufficiently reliable, yet the numbers are not without interest, for omissions occurred among adults as well as among children. It is evident, however, that neither adults nor older children enjoy in this connection any privilege denied to infants.

Epidemics have completely changed our ideas with regard to the possibility of recovery from paralysis. A little while ago it

was accepted as an axiom that a person attacked by acute poliomyelitis never completely recovered. But now it has been demonstrated frequently by clinicians in this and other countries, that a fairly extensive paralysis may absolutely disappear. The condition of the patients, reported by me as paralyzed soon after the acute stage of their illness, I tried to ascertain one to one and a half years later. The returns obtained concern 530 of them, and were as follows:

Paralyzed 297—56 per cent.
Recovered 233—44 per cent.

These figures have been given, however, only partly by physicians and partly by teachers and others. They cannot, therefore, be considered as wholly exact. They are nevertheless of interest, as they show that an unexpectedly high percentage of the paralyzed recovered without appreciable permanent disability.

Leegaard showed in his report that 26.87 per cent. of paralyzed cases got well.

Ed. Müller had 58 patients under prolonged observation; 10 of them—15 per cent.—long before the end of the first half year, recovered without obvious impairment of function. Müller states, however, that this is only the minimum figure for subsequently so marked improvement ensued in the other patients that at the date of the publication of his report severe and widespread paralysis remained only in about one third of the whole number. Those attacked in the epidemic in Westphalia who recovered without a trace of the disease were estimated by Krause to number 15–20 per cent.

Zappert reported from the Austrian epidemic of 1908, the recovery of 37 out of 266 cases. But he mentioned that the actual number of recoveries was probably greater, for between the onset of the epidemic and the commencement of the general statistical investigation only a few months elapsed. A great number of cases of marked improvement were known also to Zappert then.

Foerster, about six months after the onset of the disease, noted in fifteen cases which he observed very closely three who completely recovered and two who at the time of the report were almost well.

The collective report of the epidemic of 1907 in New York

shows a less favorable state of affairs. Only in 5.3 per cent. a complete, and in 1.8 per cent. an "almost complete" disappearance of the paralysis occurred. But even here variation occurred, for, according to Ed. Müller, Koplik, who observed part of the epidemic, indicated that recovery was the rule. He observed widespread paralysis completely disappear or persist only in limited areas.

*Age Factor in Prognosis.*—Of my 530 cases of paralysis, 384 were aged from 0–11 years. One and a half years after the onset of the disease, 198 in this age period—51.6 per cent.—were reported as still paralyzed; and 186—48.4 per cent.—as recovered. Of the paralyzed patients older than 11 years, 99 (67.8 per cent.) remained paralyzed a year and a half after the onset; and 47 (32.2 per cent.) recovered. As the percentage of recoveries is lower between the ages of 0–2 years—when disturbances of function are more readily overlooked—than between the ages of 3–11 years, the value of my figures cannot be questioned on the ground that a residuum is more evident in and to an older individual.

Leegaard reported between the ages of 0–14 years 404 cases; of them, 281 (69.6 per cent.) remained paralyzed, and 123 (30.4 per cent.) recovered.

Of the 132 paralytic cases above the age of 14, there remained paralyzed 102—77.3 per cent.—and there were cured 30—22.7 per cent.

Leegaard's statistics, as also mine, show that with respect to recovery from paralysis, adults are not so favorably situated as children.[1]

We must therefore conclude that the prognosis is in every respect more unfavorable in adults than in children.

In comparison with the age factor, none other seems to have any demonstrable effect upon the prognosis. Physical condition and neuropathic predisposition cannot be shown to have any importance either in my cases or those of others. Fatal cases often occurred among strong and healthy peasants. Exertion during the initial stage seems unfavorably to influence the further course of the disease and seems to tend to induce a relapse.

[1] My previous statements concerning the importance of age in complete recovery were based upon observations I made upon my own patients; whereas these are founded upon all the available data in the general report.

Can we from any clinical data predict the course and termination of the disease in a given case? All clinicians agree that the intensity of the initial symptoms has no prognostic significance. Alarming initial symptoms may usher in a benign or an abortive attack; and a mild beginning may be the prelude of a stormy, perhaps of a fatal course.

All text books state that electrical irritability is a prognostic index. Oppenheim asserts that muscles which show a complete reaction of degeneration, at the end of the first week, will probably remain permanently paralyzed; whereas, those in which the faradic excitability is not wholly lost after 2–3 weeks probably will regain functional activity. Although this may be the usual rule, recent experience has taught us that the issue cannot be so exactly forecasted.

From my somewhat limited electrical investigations, I have received the impression that the prevailing teaching upon the prognostic value of electrical examinations is not quite accurate and that the entire problem needs reinvestigation. Recently Ed. Müller has confirmed this impression. He found the active contraction of muscles to be much better than their electrical reactions had led him to expect; and he observed that even after weeks of persistent paralysis the reaction of degeneration might be absent. Moreover, Foerster maintains that muscles which during the acute paralysis show the reaction of degeneration may completely recover. Hence, the old law on this point should not be accepted too rigidly.

It is also of importance to know how long improvement may be expected. Most of the complete recoveries take place undoubtedly during the first half year; but some not rarely occur during the second half; and Petrén and Ehrenbergh assert that they have succeeded, by prolonged treatment, in procuring recovery of paralyzed muscles even after several years. It is now certain that improvement and recovery may be induced by correct therapy at a far later period than was believed formerly.

It is not without interest to consider whether these recently established facts relative to prognosis, which contradict earlier experience, are actually new, or are merely old features, now rightly interpreted. In discussing the identity of the epidemic with the classic sporadic poliomyelitis the difference alleged

in the prognosis of the two conditions was mentioned. No such difference, I believe, exists. We cannot deny that the mortality of poliomyelitis is subject to fluctuation. I have expressly accentuated and adduced evidence of this variability. Undoubtedly the percentage mortality of sporadic cases is much larger than has generally been accepted. Fatal cases in children hitherto have been diagnosed as meningitis. Medin and Pierre Marie record actual instances of such diagnoses. Among young children who die of acute poliomyelitis, meningitic symptoms are more marked than among older (Zappert). In former times defective knowledge of the early stage evidently led to so many errors in diagnosis that teaching concerning the mortality in classical poliomyelitis was unreliable. In adults all lethal cases were formerly diagnosed as "Landry's paralysis" which was regarded as a disease *sui generis;* whereas, we know now that most of the fatal cases of Heine-Medin's disease follow the course of a Landry's paralysis.

Referring again to the recovery from paralysis I may say that in former times such a result was certainly not unknown; and perhaps not rarely happened. When a cure did occur the case was diagnosed usually as polyneuritis, in accordance with the doctrine of the unfavorable prognosis *quoad valetudinem* in Heine-Medin's disease, and in harmony with the benignity of polyneuritis. And when in such benign cases tenderness was marked and spontaneous pain and sensitiveness on pressure over nerve trunks were present, the diagnosis of polyneuritis seemed incontrovertible. It is now established that patients may present these symptoms under the action of the virus of acute poliomyelitis, alone.

I think we may conclude that conditions have not materially changed and that the apparent difference between the old and the recent observations depends chiefly upon the inaccuracy of the former.

*Secondary Diseases.*—After an attack of acute poliomyelitis there seems to remain a certain predisposition to other organic nervous affections. A number of instances are known in which in a case of poliomyelitis has developed subsequently a chronic spinal cord affection. Usually chronic muscular atrophy (Charcot, Raymond, Vulpian, Cestan, Alessandrini and others); more rarely progressive myopathy (Cassirer, Rossi) appears. I saw a man

in Lennmalm's clinic at Stockholm who showed remains of a spinal infantile paralysis and suffered from a combined posterior sclerosis.

Crouzon recorded a case of a man who had suffered in childhood from infantile paralysis in the legs and who between the ages of 18 and 40 was attacked not less than nine times by sudden temporary paraplegia. A similar case was reported by Ballet and Dutil.

Pierre Marie described as secondary to and developing about a decade after acute poliomyelitis, what he calls "scoliose tardive."

But these cases in which, after complete recovery from acute poliomyelitis, secondary disease in later life appears are infrequent. According to Risien Russell, Potts in 1903 could collect from the literature only 37 cases.

## CHAPTER VIII

### Epidemiology

Bergenholtz was the first who observed a true epidemic. He recorded in the Swedish Public Health reports, 18 cases of spinal infantile paralysis which occurred in North Sweden in 1881. In 1887, Oxholm published the first article on this subject; it comprised five cases of paralysis which appeared almost simultaneously in a limited district of Norway. Although there is now no doubt of the nature of the five cases, Oxholm seems not to have been quite clear on the point. A small epidemic of 13 cases occurred in the south of France in 1885. Cordier in 1888 published such details as after the epidemic he was able to collect. Both publications remained unnoticed. Medin's lecture at the Tenth International Congress at Berlin in 1890, upon his observations during the first epidemic in Stockholm (43, or more correctly 44 cases), convinced everyone that spinal infantile paralysis could appear in epidemic form. Subsequently, other reports were made upon groups of cases, but only those described by Medin, 1895 (second epidemic in Stockholm, 21 cases); Caverley and Macphail, in America, 1894 (126 cases); Leegaard, in Norway, 1899 (54 cases); Auerbach, in Frankfort on Main, 1898 (15 cases); Buccelli, in Italy, 1897 (17 cases); Zappert, in Vienna, 1898 (42 cases); Platou, 1904 (20 cases), and Nonne, in Norway (41 cases), 1904, could be called epidemics. Other outbreaks consisted of groups usually of 4 or 5 cases, sometimes more, sometimes less. (Brieglieb, Andre, Pierracini, Pasteur, Pleuss, M. Taylor, Buzzard, Bülow-Hansen and Harbitz, Newmark, Packard, Chapin, and others).

No reports give us any explanation of the mode of spread of Heine-Medin's disease. The only noteworthy observation in this respect was Leegaard's. He proved that the disease showed a remarkable relation to highways. But to him, also, the precise mode of diffusion of the disease remained obscure. The current view was expressed in the sentence: "Infantile paralysis is of an

infectious, but not of a contagious nature." As a matter of fact no indisputable instance of contagion could be proved.

Wickman (1907) in his report of the Swedish epidemic of 1905 (1,031 cases), was the first to show that Heine-Medin's disease is conveyed from person to person, partly by those afflicted with the abortive type (abortive varieties had till then been overlooked), and partly by healthy people acting as germ carriers.

The disease, as has already been shown, occurred in several countries; *e.g.*, in Norway, 1905, 952 cases (reported by Leegaard, 1909); in New York, 1907, about 800 cases;[1] in Massachusetts, 1907, Lovett, 234 cases; in Massachusetts, 1908, Lovett and Emerson, 136 cases; in Lower Austria and Vienna, 1908, 290 cases (collected 1910 by Zappert); in Upper Austria, 1908, 68 cases, reported by Löcker and later by Lindner and Mally; in 1909, Styria, 433 cases (Fürntratt); in 1908, Heidelberg, 36 cases (J. Hoffmann); and in 1908, Hamburg, 22 cases (Nonne). In 1909, Germany was seriously invaded by the disease in epidemic form. In Westphalia 633 cases occurred (P. Krause); in Hesse-Nassau over 130 cases (Ed. Müller), and some smaller attacks occurred, in Hanover, 34 cases (Eichelberg), Silesia at least 50 cases (Foerster), and in Pomerania, 51 cases (Peiper). The German epidemic of 1909 comprised, therefore, at least 1,000 cases and probably more.

The disease appeared in epidemic form in France and Holland. Netter reported about 100 cases in and around Paris.

In addition to these, other epidemics prevailed in America and Australia, which, as their reports are not at present at my disposal, I cannot intimately discuss, but I shall quote Netter and Lovett concerning them.

Australia: Alston, 1895 (14 cases); Wade, 1904 (34 cases).

America: Painter, 1892 (38 cases), in Massachusetts, of which Brachett (1894) communicated 10; Bondurant and Woods in Alabama, 1900, 15 cases.

In 1908 the epidemic appeared in several States, among them Minnesota (over 150 cases), other than Massachusetts (Lovett

[1] In the general report of the American epidemic it is stated that data concerning 752 cases existed, but that the reporting committee estimated the actual figure as not less than 2,000 cases. The basis for this estimate sems to me absolutely inadequate to sustain it.

and Emerson). More than 200 cases were reported from Nebraska in 1909.

It was long recognized that acute poliomyelitis prevailed mostly during summer and early autumn. This seasonal incidence was maintained, as a rule, in the recent epidemics. Not less than 86 per cent. of the cases in the Swedish epidemic of 1905 occurred between July and October. The maximum number, 35 per cent. of the total cases, developed in August. Leegaard observed a similar incidence in the Norwegian epidemic. But the maximum of the 1907 epidemic in New York occurred in September; and in September most cases appeared in the Massachusetts epidemic described by Lovett. During the epidemic in Hesse-Nassau (Ed. Müller) the morbidity was markedly less in July, August and September than in October and November. In these last two months over 75 per cent. of the total cases occurred. Müller explains that the disease probably began in the adjacent region of Westphalia, reached its height there in September and October, and gradually invaded Hesse-Nassau till it assumed epidemic proportions. The apex of an epidemic, therefore, occurs, as a rule, in summer and early autumn; but in certain districts it has occurred in winter. In three adjacent and clearly connected outbreaks, the 18 cases of the first appeared between June and October; the 27, comprising the second, which occurred to the west of the first, from July to December; and the 72 cases of the third, which appeared in a contiguous but still more westerly district, developed between the end of September and the following February, and had their maximum during November and December (Wickman). An epidemic which prevailed throughout the winter in North Sweden has just been reported to the board of health. From October till the following September, 69 cases were observed in a relatively small area, by the only physician of the district. They occurred as follows: October to December, 13 cases; January to March, 25; April to June, 28; and July to September, 3 cases. The apex of this epidemic occurred, therefore, in April and May. Although Heine-Medin's disease may be deemed a summer malady, it may not only occur, it may be even epidemic in winter. Its winter occurrence is, as I shall later discuss, not without importance from the point of view of the mode of spread of the disease.

Wickman states that the period of incubation is one to four

days; Leegaard, one to three. The incubation period was estimated from the interval which elapsed between the first and second case in instances of multiple victims in the same family. As one to four days prevailed so markedly, it seems justifiable to accept a short incubation. But in some cases, in which apparently the disease developed after a visit, Wickman found that the incubation lasted six to ten days. As far as can be ascertained at present the last is, most likely, the true period. In six cases in which the source of infection and the duration of the exposure to infection were definitely known the minimum incubation was five days; and the average about seven. P. Krause estimates the incubation period at ten to twelve days. Experimental inoculation of monkeys has shown an incubation of nine to ten days with a minimum of four and a maximum of thirty-three (Flexner and Lewis).

But a person, who, for instance, while visiting is exposed to the disease, is not necessarily infected then. The virus may lodge on the hands, clothes, or elsewhere and only later invade the body. The actual infection dates from the invasion of the tissues and not from the exposure. These figures, especially the higher, are, therefore, not beyond criticism. But in monkeys the incubation period is calculated legitimately from the moment of inoculation to the first appearance of paralysis—for, as a rule, the characteristic initial fever observed in man is usually absent in monkeys. The difference between my estimate and the results of experimental investigation is not therefore so great as appears at first.

An incubation period of one to two days is indisputably too short. When this interval is observed between the first and the subsequent case in a family each patient must be infected from a common source. I believe that in man, if the onset of the disease be calculated from the commencement of the fever—as it should be—the incubation period will be found to be at least three to four days. Its average duration might quite probably be even higher. The acceptance of a somewhat longer period of incubation does not, in any way, weaken my conclusions concerning the mode of spread of the disease.

Wickman during the Swedish epidemic of 1905 first established the precise manner in which the disease spreads. As no opportunity so favorable has since occurred for the study of epidemic conditions, I shall give in detail the observations I made then.

The 1905 epidemic comprised 1,031 cases. Their distribution was irregular; foci of 4 or 5 or more or fewer cases were widely scattered. In the regions intervening there was either no instance of the disease or only an isolated case. These infected foci occurred in no relation to the density of the population; ravaged rural districts; and practically spared the cities. Within the large groups, it was possible to investigate minutely only restricted areas where every case was publicly known, and where the determining factor could be sought. In these areas contact between all afflicted with the disease could be proved to have taken place; whereas, no other factor which would satisfactorily explain the manner in which the malady spread, could be incriminated. The transmission may be indirect. It is not absolutely necessary for direct contact of patient with patient to occur. Indeed, the disease seems more often to be propagated through the mediation of the healthy. As in many other epidemic maladies, spread occurs in Heine-Medin's disease by transmission from person to person.

I shall demonstrate a few examples of this diffusion. Fig. 7 illustrates an outbreak within the little parish of Trästena. The parish lies some distance from the highroad and has somewhat more than 500 inhabitants. The houses, 102 in number, are dotted singly over an area of 32.5 sq. kilometers. Each house, almost without exception, is occupied by only one family. The intercourse between the individual families is limited. Each household possesses a spring and, usually, one or more cows. The products of their farming supply their simple wants, and from the outside world little enters their spheres. In such a community the spread of an infectious disease can be accurately studied.

In this parish, between June 28 and August 14, not less than 49 people, chiefly children, were attacked by acute poliomyelitis. In 26 cases paralysis resulted; in the others motility was unimpaired. The dates of affection of the latter are placed in parenthesis in the figure.

The conditions under which the people lived obviously precluded infection from either milk or water; and the only supplies which entered the parish came from a village where the disease was yet unknown.

The search for a common source of infection led to the public school of the parish. Not less than seven patients, who in their

families were the source of infection for new cases, were school children. These, Nos. 477, 463, 465, 470, 481, 459 and 472, are in the figure connected by lines with the school (*X*). In one family, where four were taken ill (477 to 480), the child first afflicted was the only one attending the school. The teacher lived in the school house with his four children. Two of them were pupils. All were attacked by Heine-Medin's disease (Nos. 455–458).

Other groups could be connected also with the school. For instance, cases occurred in five families in each of which one or more members who showed no symptoms of illness attended school. Two affected children (Nos. 498 and 499) of the same family neither attended school nor had they brothers or sisters of school age; they lived in a single story house with another little girl who went to school, but who was not ill. Each of these houses is connected in the schema by dotted lines with the school. The infection can, therefore, be shared in this as in all other infectious diseases by persons who show no morbid symptoms. Such intermediaries must act as virus carriers.

The moment of the appearance of the disease in the different families harmonized very closely with the hypothesis of dissemination by way of the school. Where the disease originated from direct infection by sick school children the first cases appeared between June 28 and July 12. But where, in all probability, the infection was carried to a family by healthy school children, the first cases occurred between July 13 and 23. The school was closed on July 15. I believe no demonstration of a school epidemic better than this could be found. Of the other cases, four or five were traced to infection at the house of Nos. 470 and 471. No. 471 was attacked on July 18; No. 484 visited him on July 19, and was taken ill on July 22. Later, the disease attacked the two sisters of Nos. 470 and 471. No. 487, a hired laborer on the premises of No. 470, became ill on July 29. A man, who had one son attacked on July 23 (case No. 497), and another a pupil, was also a hired laborer with No. 470; here the possibility of infection both from this infected house and from the school exists.

Only three of the houses attacked in this parish remain to be considered. One of these, which No. 481 occupied, was situated only a few steps from the house which was first attacked. The

two families came often in contact with each other during the outbreak. In the other cases (Nos. 500, 501, 502 and 503) no certain connection with the rest could be proved; but the disposition of the houses is such that direct or indirect infection was quite possible. Moreover, the disease appeared in these last houses at the end of July.

In all probability cases 470 and 471 were the source of infection for a small focus which developed in a little parish about one hundred kilometers from Trästena. A boy, three years old, was

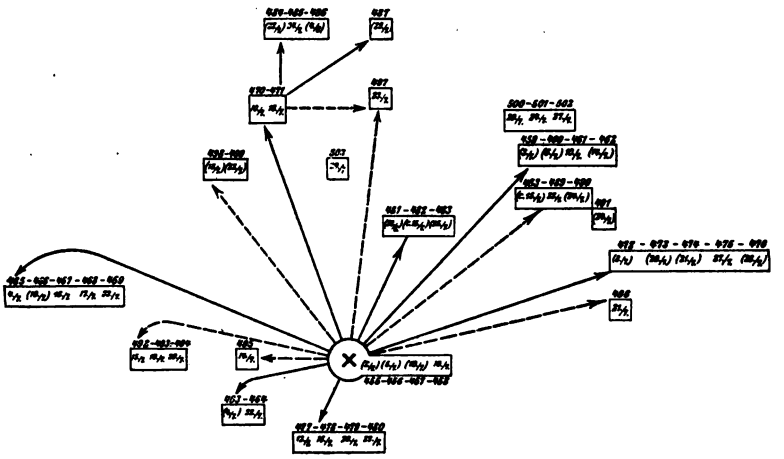


FIG. 7. School epidemic in Sweden, 1905. Each parallelogram represents a house, X is the school. The dates in parentheses represent abortive cases. The continuous lines represent the direct infection; the broken lines, the indirect infection (by personal contact).

the first victim. He travelled with his mother, on July 23, to a village, adjacent to Trästena, where his grandparents dwelt. The way led through infected districts; and while the child was at his grandparents' house, a relative came there who was employed as a servant on the farm where Nos. 470 and 471 were ill. On July 27, the boy was taken ill with the usual symptoms. On July 30, the mother set out with her sick child and on the same day arrived home. On August 17, the father of the boy was taken ill with paralysis in one leg. On August 15, a child living in their house was attacked. The next case occurred on August 21, about one kilometer from the infected house, and was followed, on August

27, by another in the immediate neighborhood. At the beginning of September the brother of the last patient was taken ill.

From Trästena the infection radiated (Fig. 8) to the surrounding districts.

Another smaller focus in which communication between nearly all the cases could be proved is depicted in Fig. 9. The local conditions in this, as in the epidemic centers about to be discussed, were very similar to those at Trästena. The spread here, also, was partly due to the school. Nos. 136 and 138 and 141 were school children. Nos. 135 and 136 lived in the immediate vicinity of the school and were accustomed to play with the school children during the recreation hour. No. 140 lived in the same house

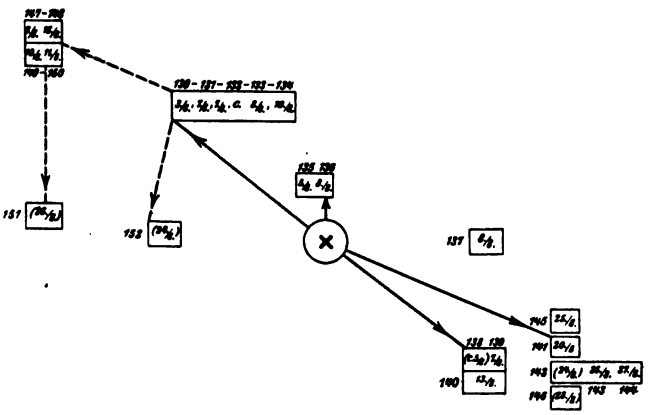


FIG. 8. School epidemic in Sweden, 1905. Explanation same as in Fig. 7.

as Nos. 138 and 139; and 142, 143, 144, 145 and 146 lived in a house only a few steps from the house of No. 141. Contact, therefore, could scarcely be avoided. The cases numbered 147, 148, 149 and 150 were distributed in two houses which lay side by side; it was established that contact had occurred between them and cases 130 to 134. A similar connection was highly probable between No. 151 and Nos. 147 to 150. No. 152 lived with his grandparents, who were servants in the household of Nos. 130 to 134. No contact to explain No. 137 could be proved. The parish contained 1,400 inhabitants. The houses were occupied usually by one family and were irregularly distributed within the parish confines.

Fig. 9 demonstrates the mode of diffusion of the disease within a group of 19 cases (9 abortive). They all occurred on two islands which lie in a large lake. The smaller island, Borgö, contributed only three cases; the larger, Sirkö, five kilometers long, and one to two kilometers broad, the others. Most of the patients were school children. One case (No. 274) could be connected with the school only through a healthy person who acted probably as a disease carrier. No. 271, an adult who worked in the fields,

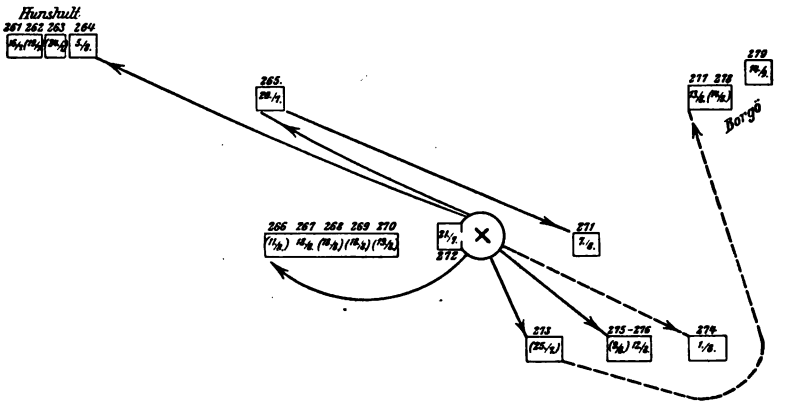



FIG. 9. Contact epidemic in Sweden, 1905. Explanation same as in Fig. 7.

took her meals during the day at the house where No. 265 was already ill.

The cases on the island of Borgö (Nos. 277–279) could be connected with those on Sirkö. The parents of the mother of the first two children attacked on Borgö lived on Sirkö, in a house adjoining that in which No. 273 became ill on July 25. Between July 25 and August 13, the father of the two children had several times visited his wife's parents at Sirkö and certainly encountered the relatives of No. 273. For the remaining case at Borgö these two were evidently the source of infection; their dwellings were near one another. Between almost all the cases contact could be proved. The longer island is inhabited by 28 families who occupy 29 houses. One-family dwellings are therefore the rule.

It was impossible to find how the disease penetrated the island. Only one point was assured; the father of the children who were attacked first was the only person who kept actively in touch with the surrounding mainland.

Fig. 10 shows another example of a school epidemic. This center contained 18 cases; ten of these were abortive and presented pronounced general symptoms. Ten of the eighteen attended school; one (No. 328) of the ten and his brother dwelt in the schoolhouse with the teacher's son. The school was closed on September 19; two cases subsequently occurred—one on September 22 and one on September 29. Only for six children, occupying four houses, could no contact with the other 52 who attended school be traced. The parish comprises over 3,000 inhabitants.

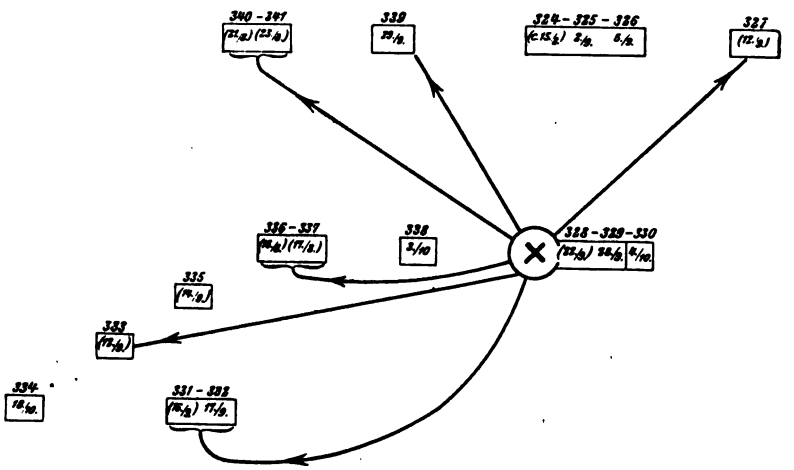


FIG. 10. School epidemic in Sweden, 1905.

Lastly, I shall mention another small epidemic center (Fig. 11). A woman, 54 years old, was attacked first (No. 714). She probably became infected in a district where the disease was epidemic, about five kilometers from her own village. Her illness began on December 5. Her son (No. 715), 22 years old, was taken ill on December 13. On December 18, a man servant (No. 716) who lived about two kilometers away, and who had several times visited the sick No. 715 was attacked. On December 24 a little girl of four years was taken ill in the household of No. 716. Two cousins of the child lived only a stone's throw away and were daily with her; they were taken ill on December 26, 1905, and on January 1, 1906, respectively. One of the cousins developed fever, severe pains in the neck and opisthotonus, but recov-

ered without paralysis. Two cases seemed to be infected through the intermediation of a healthy carrier of the disease. In their family a housekeeper was employed who was the sister of No. 716 and who had visited him daily for a week during his illness. She herself showed no morbid symptoms, but the two children (cases 720 and 721) of the family were taken ill on December 31, 1905, and January 10, 1906, respectively. Case 720 showed only

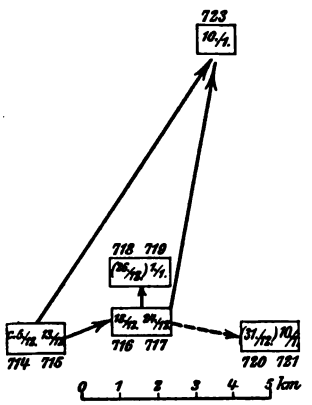



FIG. 11. Small focus, showing evident contact between the cases.

general symptoms and rigidity of the neck. An adult who lived about 10 kilometers from this neighborhood was taken ill on January 10. He had spent Christmas and the early part of January at his parents' house close to cases No. 716 to 719. He visited No. 715 first on January 3; subsequently, he often visited both No. 715 and 716.

The country where this group of cases occurred is sparsely peopled. But in the vicinity of the attacked dwellings, a number of houses are situated. It cannot therefore be regarded as accidental that the disease afflicted only such persons as stood in the relation to each other which I have just traced. The possibility of the transmission of the disease from house to house by means of healthy carriers was proved in numerous other groups, also.

These small centers were part of large foci in which it was impossible always accurately to trace the mode of spread of the disease. Yet regarding these large foci certain facts are noteworthy.

The infection seemed to radiate, as a rule; the cases occurred in groups; and in many of the scattered cases the possibility either of direct or of indirect transmission existed. The tendency to arrangement in groups was expressed by the disease implicating members of one family, dwellers in one house, or persons living in neighboring houses. The 1,031 cases were distributed as follows:

| | | | |
|---|---|---|---|
| In each of | 627 | houses | 1 case occurred. |
| In each of | 95 | houses | 2 cases occurred. |
| In each of | 39 | houses | 3 cases occurred. |
| In each of | 14 | houses | 4 cases occurred. |
| In each of | 7 | houses | 5 cases occurred. |
| In | 1 | house | 8 cases occurred. |

These figures seem high compared with statistics of others, but abortive cases are here included. All abortive cases were omitted, however, except 157, which occurred in restricted areas where the diagnosis could be proved beyond cavil. If all the abortive cases were included the resemblance to a contagious disease would be greater still.

The distinct group-like disposition which the cases showed within the larger foci was analogous to an attack involving several members of one family. The chronological order of the cases within the smaller groups showed that probably the disease resulted from a causal agent common to them all.

Another important observation was the radiate nature of the dissemination within the focus itself which I have illustrated by remarkable examples. In still other districts as the groups appeared about the same time they were infected probably from the same source.

Fig. 12 demonstrates foci with radiate spreading. The disease appeared here first about June 30, on a large estate, Stora Sundby, which is renowned for its natural beauty and is a favorite tourist resort. On June 23 and 24, Sweden celebrates great national festivals. The disease was epidemic to the west of Stora Sundby. Stora Sundby itself was free before the holidays occurred. Excursionists probably brought the infection with them and an outbreak followed. The figure shows how the disease spread in various directions. Towards the north lies the small borough of Kungsor, in which 13 cases occurred. The son of

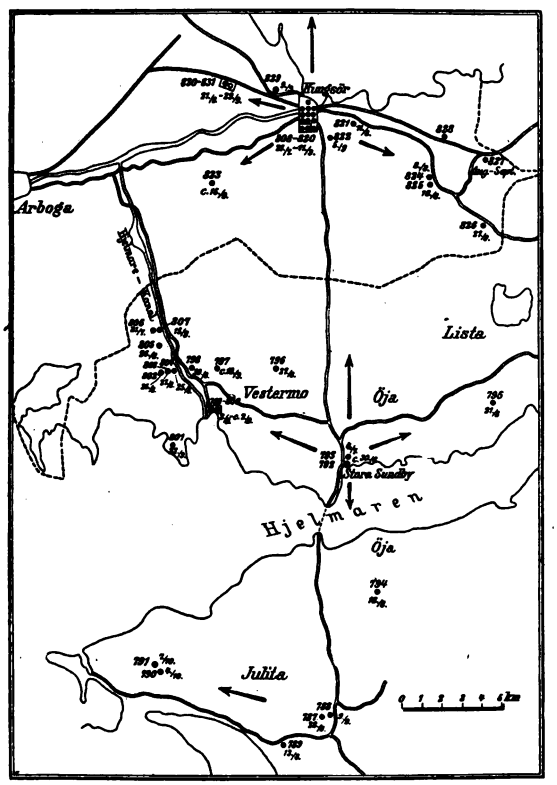



FIG. 12. Focus with radiate spreading, Sweden, 1905.

the only physician of the place was the first afflicted. The physician, undoubtedly, may have transmitted the disease to some of the others attacked. From Kungsor diffusions in all directions took place. Every case shown in the figure presented paralysis. In some, direct contact could be traced. In response to our inquiries the physician reported that he had observed a number of cases which completely recovered and which showed exactly the same symptoms as occurred in the initial stage of the illness of those who developed paralysis. Undoubtedly, therefore, abortive cases occurred also, and the epidemiological conditions of a contagious disease might have been demonstrable here if attention had been paid to these abortive cases and to the virus carriers. These conditions were partly established later. The patient mentioned on page 75, who died with meningeal symptoms, was suspected of eclampsia and had premature labor induced. The woman was taken ill on August 19. Two days previously, her son had been attacked with fever and great drowsiness. It was alleged that he developed no paralysis then; as a year afterwards, his left leg was thinner than his right, possibly in the acute stage, the paralysis was overlooked. On August 24 the midwife, who took care of the woman and assisted at the confinement, became ill with headache, pain in the back, arms, and legs, nausea, and high fever. She recovered without presenting any signs of paralysis. The boy and the midwife probably were abortive cases (unless the boy be regarded as a paralytic case).

The intimate association of the disease with the principal highways was clearly demonstrable. The relation to main roads and railways was especially striking in districts in which the cases were scattered, either singly or in small groups. A study of the local conditions showed that dissemination must be due to the busy traffic which permitted more frequent communication between the people.

The Swedish epidemic of 1905 thus demonstrated that the mode in which the disease spreads both within the large epidemic centers and within the individual components which constitute them, so far as it was possible to determine, was essentially analogous to that established for a number of other infectious diseases, in which transmission takes place from person to person.

Acute poliomyelitis must, therefore, be included among the con-

tagious diseases. The lateness of the recognition of this fact is due partly to the smallness of former epidemics and partly to two factors which nullified all earlier investigations of epidemic conditions; viz., first, abortive types were not considered, and, second, the possibility of infection through healthy virus carriers was not realized.

It was rarely probable that infection was conveyed by food or by inanimate objects. The following instances I observed during the 1905 epidemic in Sweden. They are reported now for the first time. In a certain district three cases appeared in one family; two cases in each of two others; altogether six families were attacked and ten cases occurred. The first patient was a farmer's son who was attacked on October 20; his brother and four children of the neighborhood were seized with the same symptoms. All the patients were supplied with milk by the farmer. The houses were separated from one another by one to two kilometers; and in five cases the illness began on the same day. Under these circumstances it seems to me extremely probable that the milk convyed the infection.

In exceptional cases the infection seems to be carried by inanimate objects, also. An adult who was taken ill near Stockholm on July 27 acquired paralysis of a leg. Sometime after, she was transported to her home in Stockholm. During her convalescence she amused herself with sketching and similar work. Early in September one of her drawings was sent to a studio to be reproduced. At the studio the person who performed this work, a lady, 34 years old, was taken ill on September 25 and suffered from a typical acute poliomyelitis. This lady was the only person in the studio who was affected; the population of Stockholm is almost 300,000; in the year in question only 11 cases of Heine-Medin's disease were reported from Stockholm; and the lady had been exposed to no other source of infection. Such cases are of great rarity. They do not prejudice in any way the doctrine of the contagious nature of acute poliomyelitis; analogous cases are known to happen in all other infectious diseases.

Our observations in the Swedish epidemic of 1905 have not always been corroborated by those who have studied subsequent outbreaks elsewhere. But no other manner of spread has been demonstrated; and corroboration was usual when the reporter

himself had clinically investigated the cases. Yet Leegaard, who apparently confined his efforts to editing the accounts he received of the Norwegian epidemic, concludes that the disease is transmitted from person to person; and that the infection is conveyed more often by healthy carriers than by direct contact with the sick; and he adduces many examples in support of these conclusions.

In Westphalia P. Krause occasionally observed distinct foci of the disease which were particularly linked to certain roads. He, also, was able to prove transmission through intermediate persons who remained well. But, on the other hand, he exonerates food, water, milk, insects, etc.

From the epidemic in Hesse-Nassau Ed. Müller, who thoroughly studied it, concluded that Heine-Medin's disease is contagious, and that it is spread less often by the affected children than by the healthy disease carriers. Müller reports several instances in which persons carried the disease from infected to non-infected districts; and instances, also, in which healthy persons had, for a short time, visited an infected locality, then returned home and spread the virus among their own community. In many villages intercourse between infected houses was traced. It is noteworthy, as Ed. Müller remarks, how the first and often the only case of poliomyelitis in an otherwise healthy people occurred, as a rule, not among the real peasantry but in a family of a person who had business relations with people outside the parish; *e. g.*, an innkeeper, a coachman, a letter carrier or a shoemaker. To both Müller and Eichelberg the morbidity among shoemakers' children seemed particularly striking. These observers think that the infection possibly lurks in the dirt which adheres to personal belongings, such as clothing, shoes, etc., of the intermediate carrier. The connection of the first cases with highroads and railways Müller could trace invariably; whereas, localities far from the principal communication routes remained free from invasion. Ed. Müller's observations are especially interesting, for the epidemic he studied consisted of a dense aggregation of isolated cases. If his investigation had not been so thorough the dissemination of the infection would have appeared mysterious and inexplicable.

Each of a small group of seven cases investigated by Netter

dwelt far from, and had no dealings with, the others; but three of them, the brother of a fourth, and the cousin of a fifth all attended the same school.

The epidemic in Austria reported by Löcker also seems to have been due to contact. Most of the cases appeared in isolated and remotely situated houses. Yet, large and smaller groups occurred; and Löcker proved in several districts that the school played a great part in spreading the disease. Indeed, in one locality, practically all the affected children were pupils of the parish school. The local conditions in this epidemic greatly resembled those in several of the Swedish districts, in which food and water as sources of infection could be excluded. Lindner and Mally investigated also this epidemic and greatly amplified Löcker's description of it. They advanced a number of proofs to show that infection here took place by contact.

Emerson proved contact between the cases in the epidemic of 1908, in Massachusetts; and Armstrong, in that of 1909, at St. Paul. Jones reported 86 cases in the Massachusetts epidemic of 1909 and stated that most of them were connected with the highways. In thirteen of the nineteen cases, which occurred within 34 days at Great Barrington, he traced some association with the school. Five of the thirteen were pupils; the rest were sisters, brothers or other relatives who were in daily contact with the pupils.

Shidler's observations (quoted by Holt) correspond closely with my own. He reported an epidemic of more than 200 cases in Nebraska. In six families, two children were attacked; in five, 3, in three, 4; and in one, 6. Remarkable proof of infection was given. The first case in the town of York was a child, who was attacked by the disease nine days after his mother and his brother returned from visiting an afflicted family in another town. All the children of a neighboring family were taken ill soon afterwards. A child visited this family and was attacked five days later. A boy, who lived outside the town, visited the affected locality, became ill, and was transported back to his home in the country. His sister was attacked then. A few weeks later a child from another town, where no cases were known, visited this country family and stayed over night. Five days later he, also, was taken ill. A month passed and then another child spent a

night with the same family; he likewise became ill five days afterwards. Shidler is stated to have reported numerous other instances of infection.

There still remain many epidemics in which contagion could not be established, but in which some of the features we have been discussing, such as the occurrence of the cases in groups, and the distribution of the disease along the channels of communication, were present. Among these is the epidemic of 1908 in Vienna and North Austria which was described by Zappert. The disease raged in a thickly populated province, traversed by many trade routes. To investigate the epidemic conditions here was therefore no easy task. Yet, Zappert was able to establish the following suggestive facts: The 129 cases in Vienna showed a very irregular distribution; the case incidence did not vary as the density of the population; and within any one district the cases tended to accumulate in certain quarters and houses. But, on the other hand, the relation of the cases to each other could be just as little demonstrated as their radiation from a common center. Zappert collected 137 cases in North Austria. Here also the disease showed no uniform distribution but more distinctly and obviously than in Vienna the cases developed in groups. Zappert concluded it would be incorrect to deny that the disease is contagious, although he failed to prove contagion in this epidemic.

Zappert's statements regarding the discordant time relations of the various groups of cases are very interesting. He found the group of early cases occurred in Lower Austria in every district which bordered Vienna on the south and west; the groups of later cases developed in the north of the province; whereas, the September and October cases appeared in the center and in part of the southern division of Lower Austria. Zappert seems here to establish a very pretty succession of groups. However, he asserts that in spite of the evident and striking distribution of the cases, no clue could be found to any underlying factor determining the path of the epidemic. He bases this assertion, so far as I can judge, principally upon the fact that the early cases occurred at the northwest, whereas the later appeared at the southwest boundary of the province. I believe one ought not to ascribe such great importance to cases appearing—so to speak—outside the epidemic, on the boundary of Bohemia and Hungary. As very imperfect re-

ports of the cases of poliomyelitis were issued from these countries, one cannot affirm that the disease there was not connected with the other foci of the epidemic. Moreover, in densely populated districts with busy traffic an epidemic passes not as a running stream, which always must flow through one region before it can reach the next; an epidemic spreads by "leaps" and we must expect such "leaps."

I am inclined to ascribe much more importance to the distribution of the cases and to the time relation shown in the succession of the groups than Zappert cares to admit.

Lovett, whose report on the Massachusetts epidemic of 1908 was similar to Zappert's, also, found a distinctly perceptible formation of the cases in groups. These groups occurred along the railroad and the disease tended especially to spread along the lines of greatest traffic. Lovett observed among the 134 cases of the epidemic, eleven instances in which the disease attacked more than one dweller in the same house; and 20 in which acquaintances of sufferers were attacked. He estimated that the possibility of transmission was demonstrable in 17 per cent. of cases. On the other hand Lovett inclines, without valid proof, to accept that the virus may occur in milk. But there are observations (New York epidemic of 1907) to show that the disease is prevalent among breast-fed babies; and my own work, also, tends to show that we may exclude not only milk but even food as a source of infection. The epidemics in New York, in 1907; in Styria, in 1909 (Fürntratt); and in Pomerania (Peiper), give no positive information regarding the mode of spread. No method of dissemination could be established in these, other than that I advocate. Fürntratt stated that at the onset of the epidemic he could confirm my observations, whereas, later, he could do so only guardedly. Peiper found at least one instance of aggregation of the cases into groups but could not trace the infection either directly or by healthy carriers.

It has been pointed out in opposition to my contention that acute poliomyelitis is contagious, that the disease appears only sporadically; that during an epidemic only one member of a family may be affected, even if adequate opportunity for infection be offered to the others; and that infection in hospitals has not been observed. These are the principal objections. How very little

is their worth, I can best show by analogy. We do not need to go far into the past to encounter the time when exactly the same arguments were quoted against the contagious nature of cerebrospinal meningitis. Here, also, it had been observed that only one child in a family was attacked; that a healthy child might share his bed with impunity; and that no hospital infections occurred. Probably, no human being doubts now that cerebrospinal meningitis is a contagious disease, since the carrier of the micrococcus has been demonstrated and contact chains have thence been woven. Precisely analogous conditions prevail in Heine-Medin's disease and neither the one nor the other differs from contagious diseases in its mode of spread. The only distinction which does exist is that for other infectious diseases, such as diphtheria, people show greater susceptibility than for either cerebrospinal meningitis or Heine-Medin's disease. The epidemic factors in these last two diseases are very similar. Thus from the New York epidemic of 1907 it was reported that the occurrence of several cases in one family or in one house was observed in the same percentage of cases, as in the outbreak of cerebrospinal meningitis which prevailed there in 1905. Netter, during an epidemic of cerebrospinal meningitis affecting more than 180 cases, only five times observed more than one case in the same family or in the same house.

I wish to refer to the possibility of spread by means of insects. P. Krause and Ed. Müller excluded it, after duly weighing the evidence they had collected. The prevalence of Heine-Medin's disease in summer may be adduced as suggestive of this mode of spread. But, on the other hand, insects could not promote the continuance into the winter months which occasionally occurs. One of the most striking of the winter epidemics, so far as this point is concerned, was the north of Sweden epidemic to which reference has already been made. There the snow begins to melt only in May and the temperature at the time of the scourge was far below zero.

Various authors have also established that Heine-Medin's disease in epidemic form never afflicts the same district two years in succession. Some insect-carried diseases, such as malaria, recur annually with unabated virulence.

Moreover, hardly any disease disseminated by insects could show such evident contagious characters as have been observed in certain epidemics of acute poliomyelitis.

Caverley, Wickman, Peiper, and others have mentioned the appearance of paralysis in animals and in fowl coincident with epidemics among human beings. But the futile inoculation of these creatures shows their affliction has nothing in common with that in man.

Recurrence of acute poliomyelitis in a house after a period of one or more years has been reported by Wickman, Fürntratt, J. Hoffmann. It is impossible to determine in such cases whether the virus has remained active or a fresh infection has been introduced.

The general trend of the results of recent investigation has been to confirm my observations concerning the contagious nature of acute poliomyelitis. Particularly has this been the case in epidemics in which the abortive type and, above all, the healthy disease carriers have been considered. But in several other epidemics also one can recognize some of the chief characteristics of a contagious disease.

If recording physicians had personally made all observations and if accompanying circumstances had not so greatly complicated the problem the result would have been more conclusive. Yet, Jaeger's words concerning cerebrospinal meningitis may not inappropriately be applied to acute poliomyelitis. "The diffusion of this scourge appears to us now like a mountain range free from mist; only peaks without foundation are visible; yet we are perceiving now more and more the great bases upon which the peaks arise." The more exactly we study epidemics of Heine-Medin's disease the more apt will Jaeger's words appear.

## CHAPTER IX

### Prophylaxis and Therapy

As a logical consequence of the doctrine of the infectivity of Heine-Medin's disease physicians and public authorities should enforce the same regulations for the prevention of this as for the prevention of other acute infectious maladies; *e. g.,* isolation of the patient, disinfection, etc. Isolation is almost insuperably difficult to attain. Not only the paralytic, but also the abortive cases, and the healthy virus agents need to be segregated. To the last two categories we possess no guides comparable with those we can utilize, for instance, in diphtheria, cerebrospinal meningitis and other contagious diseases. Hence, effective isolation practically cannot be accomplished. Under such circumstances we can only warn those suspected of being either abortive cases or virus carriers of the menace they may be to the community. Schools ought to be closed for several weeks. Isolation of the patient seems not to be essential, for experience has taught us that infection is seldom direct. The patient may, however, become a source of virus carriers and to guard against this possibility isolation is desirable. Isolation hospitals are the best means of segregating such cases, but the present custom of admitting fresh cases among others seems to me to be bad. We have no exact information yet concerning the isolation time necessary. According to Ed. Müller it is eight weeks. Most physicians in the Swedish epidemic were content with three weeks. At present we cannot, however, make any positive pronouncement on this point. Obviously an attempt must be made to destroy the infecting germs, even although we are still in the dark concerning them. Experimental poliomyelitis in monkeys has shown that we may deem the intestinal and nasal mucosæ and the salivary glands as excretory channels for the virus. It is therefore advisable at least in the early stages to disinfect the intestinal and nasal discharges. Flexner and Lewis found that one per cent. solution of hydrogen peroxide destroys the virus; such a solution may be

used to disinfect the naso-pharynx. Levaditi and Landsteiner recommend for the same purpose a one per cent. solution of menthol, or a powder of the following composition:

| | |
|---|---|
| Menthol | 0.2 grams, |
| Salol | 5.0 grams, |
| Boric acid | 20.0 grams. |

Special attention must be devoted to the disinfection of handkerchiefs in all maladies in which the germs are present in the nasal discharge, but this attention is particularly essential in Heine-Medin's disease. According to Römer formalin is sufficient for disinfecting houses.

Preventive inoculation has been attempted because of the promise of the immunity experiments to which reference has already been made. Several investigators have succeeded in making monkeys insusceptible to the virus of poliomyelitis. Landsteiner and Levaditi were able to produce by subcutaneous injection of spinal cord substance, dried as in the Pasteur method of attenuating rabies virus, a substance which protected against subsequent injections. This immunity was obtained by the subcutaneous injection of a mixture of the virus and the serum from a sheep, which previously had been treated with virulent emulsions of poliomyelitic cords. Römer and Joseph by means of a virus-serum mixture succeeded in establishing a resistance to subsequent inoculation with unaltered virus. Römer further obtained analogous results by heating the virus to 45–50° Celsius, and Krause by treating it with 0.5 per cent. carbolic acid, before injecting it subcutaneously. These are interesting experiments but their practical value has not yet been determined. Inoculation in the manner of the Pasteur method is not without danger and occasionally results in paralysis.

*Therapy.*—As no specific therapy is yet available, treatment in the acute stage must be purely symptomatic. The characteristically excessive tenderness demands the greatest possible freedom from disturbance and the most comfortable position for the patient. A plaster-of-paris jacket (Hohmann) and a plaster bed (Machol) have been recommended to ensure rest. But I agree with Ed. Müller that surgical contrivances in the early stages are superfluous. The nerve irritative phenomena soon disappear in

most cases, and may be treated with internal remedies without apparent detriment to the patient. Usually preparations such as sodium salicylate, antipyrin, and phenacetin are administered. In some cases these drugs are efficacious; in others they are not. Because of the severe pain morphine has been given. Allen Starr recommended the use of urotropin; the local antiseptic affect from the formaldehyde which urotropin liberates in the cerebrospinal fluid was desired.

Some advocate diaphoresis. I join with Oppenheim in advising that sweating be produced, not by baths which necessitates moving the patient, but by packs, hot drinks, etc.

Retention of urine, constipation, and diarrhea should be remedied in the usual way. Treatment by lumbar puncture has been used by Petrén and Ed. Müller. Ed. Müller recommended it for the relief of pressure in rapidly progressing paralysis; and especially in the meningeal type of the disease.

During the reparation stage attention is especially directed to avoiding the development of contractures. Precautions must early be taken. We must see that the bedclothes do not press upon the patient's feet. The feet should be kept at right angles; and the legs extended by splints, bandages, etc. Physicians undoubtedly are careless in this matter, and they thus enhance the difficulties of the orthopedist's task.

Besides preventing such sequelæ as contractures, active physical treatment should be commenced. Bathing, massage, passive and active movements, and electrical stimulation may be useful.

How soon should such active treatment begin? In most cases at the end of the second or third week active treatment may be initiated without harm to the patient. Resorption and reparation are then occurring and I hardly think that further advance need be feared. The chief aim of the baths is to improve the general condition. For this purpose ordinary warm water baths are used, but brine, mud, or chalybeate baths may later be serviceable. The treatment most effective in restoring the tonicity of the muscles is massage, to which passive and active movements are powerful adjuvants. Passive movements not only improve the circulation in the muscles, but also help to prevent the occurrence of contractures. Active movements must be adjusted to the degree of paralysis. If only a paresis be present, resistance movements can

be employed from the beginning. Manual resistance is at first preferable as it can easily be graduated to correspond with the strength of the muscles. Later, apparatus for exercising may be used. But if the paralysis be severe, treatment by gymnastic exercises becomes more difficult. In such cases the gymnastic treatment should be practised in baths. Or the movement which normally is subserved by the paralyzed muscle may be passively imitated while the patient attempts actively to perform it. By such treatment, contractures of years' duration, in completely paralyzed and contractionless muscles, have gradually disappeared. We ought, therefore, to practice rational physical therapy as early, as thoroughly, and as continuously, as possible.

Even if we fail to procure recovery, we can at least pave the way for the subsequent orthopedic treatment to restore function. This manual treatment must be performed by one whose hand is skilled.

Electrical treatment has long been lauded both for spinal and for muscular troubles. I doubt if it has caused any material benefit. In any case, this method of treatment is not to be compared in efficacy with the others. It often causes great uneasiness in children and it is questionable if its value materially compensates for the mental stress it involves. If electrical treatment be employed it should be used according to the principle earlier mentioned; if no faradic reaction can be elicited, naturally only the constant current should be employed.

It is difficult to state how long one ought to continue mechanical and electrical treatment. Probably no essential gain can be expected from these methods if improvement is not noticeable in a few months. This improvement occurs usually towards the end of the first year, often earlier, occasionally later (Risien Russell, Petrén). Orthopedic surgery is our next resource. In general, it is better to consult a surgeon too soon than too late. As a suitable operation places paralyzed muscles under better functional conditions it aids and quickens the recovery of their power. The necessary procedures, immobilization of joints, tendon transplantation, plastic operations on nerves, bandaging, etc., belong to the field of orthopedic surgery and mechanical orthopedy.

## LITERATURE


Achard and Grenet, Paralysie infantile et lymphocytose arachnoidienne. Rev. neurol., 1903.

Achard and Lévi, Radiographie des os dans paralysie infantile. Nouv. iconogr. de la Salp., 1897.

Alessandrini, P., Les atrophies musculaires tardives consécutives à la paralysie spinale infantile. Nouv. iconogr. de la Salp., 1909.

Andersson, C. A., Report of an epidemic of two hundred and seventy-nine cases of acute poliomyelitis. Pediatrics, 1910.

André, in Verhandl. d. med. Kongr. in Bordeaux, 1895.

Armstrong, J. M., A small epidemic of seventeen cases of poliomyelitis. Pediatrics, 1910.

Auerbach, S., Über gehäuftes Auftreten und über die Ätiologie der Poliomyelitis anterior acute infantum. Jahrb. f. Kinderheilk., 1899.

Babinski and Nageotte, Contribution à l'étude du cytodiagnostic du liquide cephalorachidien dans les affections nerveuses. Bull et mém. Soc. méd. des hôpit., 1901.

Ballet and Dutil, De quelques accidents spineaux déterminés par la présence dans la moelle d'un ancien foyer de myélite infantile. Rev. de méd., 1884.

Barnes, S., and Miller, A case of acute poliomyelitis. Brain, 1907.

Batten, F. E., The pathology of infantile paralysis (acute anterior poliomyelitis). Brain, 1904.

Baumann, Beiträge zur Kasuistik der Poliomyelitis anterior acuta. Monatsschr. Psych. u. Neurol., 1905.

Benecke, Über Poliomyelitis acuta, Münchner med. Wochenschr., 1910.

Beyer, in Neurol. Centralbl., 1895.

Bézy, P., Un cas d'encéphalite aïgue et deux cas de poliomyélite antérieure aïgue chez les enfants. Arch. méd. de Toulouse, 1907.

Bickel, O., Ein Fall von acuter Poliomyelitis beim Erwachsenen unter dem Bilde der aufsteigenden Paralyse. Diss. Bonn, 1898.

Bing, R., Beitrage zur Kenntniss der endogenen Rückenmarksfasern beim Menschen. Arch. f. Psychiatrie, 1905.

Bramwell, B., Analysis of 76 cases of poliomyelitis anterior acuta. Clinical Studies, 6, 1908.

Briegleb, E., Über die Frage der infektiösen Natur der akuten Poliomyelitis. Inaug. Diss., Jena, 1890.

Bonhoff, H., Zur Ätiologie der Heine-Medinschen Krankheit. Deutsche med. Wochenschr., 1910.

Brorström, Akute Kinderlähmung und Influenza. Leipzig, 1910.

Buccelli, Paralisi spinale e cerebrale infantile a forma epidémica. Policlinico, 1897.

Bülow-Hansen and Harbitz, Beitrag zur Lehre der akuten Poliomyelitis. Zieglers Beitr. z. Path. u. path. Anat., 1899.

Buzzard, Certain acute infective or toxic conditions of the nervous system. Lancet, 1907.

Buzzard, Th., A clinical lecture on cases illustrating the infective origin of infantile paralysis. Lancet, 1898.

Cadwalader, W. B., Acute anterior poliomyelitis. Contributions from the Department of Neurology and the Laboratory of Neuropathology (University of Pennsylvania), 1908.

Calabrese A., Contributo allo studio della paralisi infantile. Reforma med., 1903.

Camus and Sézary, Poliomyélite antérieure aïgue de l'adolescence à topographie radiculaire. Rev. neurol., 1907.

Carles, Sur quelques cas deé paralysie des muscles de la paroi abdominale au cours de la poliomyelite anterieure aïgue. Gaz. heb. des Sc. med. de Bordeaux, 1908.

Carles, Sur quelques cas de scoliose liée a l'existence de la paralysie infantile. Revue d'orthop., 1909.

Cassirer, R., Fall von abgelaufener Poliomyelitis und Muskelatrophie. Neurol. Centralbl., 1898.

Caverley, History of an epidemic of acute disease of unusual type. Med. Rec., 1894.

Cestan, Tremblement héréditaire et atrophie musculaire tardive chez un malade porteur d'un foyer ancien de paralysie infantile. Progrès méd., 1899.

Cestan and Huet, Contribution clinique a l'étude de la topographie des atrophies musculaires myélopatique. Nouv. iconogr. de la Salp., 1902.

Cestano-Savini and Savini. Zur Kenntnis der pathologischen Anatomie und der Pathogenese eines unter dem Bilde der aufsteigenden Landryschen Paralyse verlaufenden Falles von Poliomyelitis acute beim Kinde. Arch. f. Psychiatrie, 1909.

Chapin, Epidemic paralysis in children. Journ. of Amer. Med. Assoc., 1900.

Charcot and Joffroy, Cas de paralysie infantile spinale avec lésions des cornes antérieures de la substance grise. Arch. de physiol. norm. et pathol., 1870.

Charcot, Leçons sur les maladies de système nerveux. Paris, 1877.

Cordier, S., Relation d'une épidémie de paralysie atrophique de l'enfance. Lyon méd., 1888.

Cornil, V., Paralysie infantile. Compt. rend. Soc. biol. à Paris, 1863.

Coulter, F. E., Additional observations on acute poliomyelitis. Pediatrics, 1910.

Crouzon, O., Return of paraplegia in a case of old infantile paralysis. Rev. of Neurol. and Psychiat., 1907.

Cruchet, R., Sur un cas de paralysie infantile à forme monoplégique brachiale. Arch. gen. de méd., 1905.

Cruchet, R., Étude critique sur les rapports de la méningite cérébrospinale et de la paralysie infantile. Journ. méd. franc., 1910.

Dauber, Zur Lehre von der Poliomyelitis anterior acute. Deutsche Zeitschrift f. Nervenheilk., 1893.

Déjerine, Sémiologie du systém nerveux. In Traité de la pathologie générale. Bouchard. Paris, 1901.

Déjerine and Huet, Contribution a l'étude de la paralysie atrophique de l'enfance a forme hémiplégique. Arch. de physiol. norm. et pathol., 1888.

Duchenne (De Boulogne), D'éléctrisation localisée. Paris, 1855.

Duchenne fils, De la paralysie atrophique graisseuse de l'enfance. Arch. gen. de Med., 1864.

Dupre and Huet, Paralysie spinale infantile localisée aux muscles du groupe radiculaire supérieure de plexus brachial. Rev. neurol., 1902.

Duquennoy, P., Sur une forme a début douloureux de la paralysie infantile. Thèse de Paris, 1898.

Edwards, F., Contribution a l'étude de la paralysie spinale aïgue de l'adulte et de sa nature. Thèse de Paris, 1898.

Eichelberg, F., Über spinale Kinderlähmung. Deutsche med. Wochenschr., 1910.

Eisenlohr, C., Über akute Bulbär- und Ponsaffecktionen. Arch. f. Psychiatrie, 1879.

Eisenlohr, C., Pathologie und pathologische Anatomie der spinalen Kinderlähmung. Deutsche Arch. f. klin. Med., 1880.

Emerson et Lovett.

Erb, W., Über akute Spinallähmung (Poliomyelitis anterior acuta) bei Erwachsenen und über verwandte spinale Erkrankungen. Arch. f. Psychiatrie, 1875.

Erb, W., Poliomyelitis acuta superior. Deutsche med. Wochenschr., 1906.

Flexner, S., and Lewis, P. A., The transmission of acute poliomyelitis to monkeys. Journ. of Amer. Med. Assoc., 1909.

Flexner, S., and Lewis, P. A., The transmission of epidemic poliomyelitis to monkeys. A further note. Journ. of Amer. Med. Assoc., 1909.

Flexner, S., and Lewis, P. A., The nature of the virus of epidemic poliomyelitis. Journ. Amer. Med. Assoc., 1909.

Flexner, S., and Lewis, P. A., Epidemic poliomyelitis in monkeys. Fourth note. Journ. of Amer. Med. Assoc., 1910.

Flexner, S., and Lewis, P. A., Epidemic poliomyelitis in monkeys. Fifth note. Journ. of Amer. Med. Assoc., 1910.

Flexner, S., and Lewis, P. A., Experimental epidemic poliomyelitis in monkeys. Journ. of Amer. Med. Assoc., 1910.

Flexner, S., and Lewis, P. A., Experimental epidemic poliomyelitis in monkeys. Seventh note. Journ. of Exper. Med., 1910.

Foerster, Ottfried, Ein Fall von Poliomyelitis im obersten Halsmark. Allg. med. Zentralztg., 1902.

Foerster, Ottfried, Zur Symptomatologie der Poliomyelitis anterior acuta. Berliner klin. Wochenschr., 1909.

Forssner und Sjövall, Über die Poliomyelitis acuta samt einen Beitrag zur

Neuronophagienfrage. Zeitschr. f. klin. Med., 1907. Festschrift für S. E. Henschen.

Fürntratt, K., Über Poliomyelitisepidemien mit besonderer Berücksichtigung der diesjährigen Epidemie in Steiermark. Das österr. Sanitätswesen, 1909.

Van Gehuchten, A., Cas de poliomyelite anterieur aigue de l'adulte Névraxe, 1904.

Geirsvold, Epidemisk poliomyelit. Norsk. Magaz. f. Laegevid., 1905.

Goldscheider, A., Über Poliomyelitis. Zeitschr. f. klin. Med. 23, 1893. Mit Anhang von Kohnstamm.

Gowers, W. R., Handbuch der Nervenkrankheiten. Bonn, 1892.

Grober, J., Zu der rheinisch-westfälischen Epidemie von spinaler Kinderlähmung. Med. Klin., 1909.

Grober, J., Die ackute epidemische Kinderlähmung. Fortschritte der deutsch. Klin., 1910.

Guinon and Paris, Paralysie infantile avec reaction meningeé. Bull. et mém. Soc. méd. des hôpit., 1903.

Harbitz, Fr. and Scheel, O., Pathologisch-anatomische Untersuchungen über akute Poliomyelitis und verwandte Krankheiten von den Epidemien in Norwegen 1903 bis 1906. Vidensk. Selsk. Skr. Christiania. 1907.

v. Heine, J., Beobachtungen über Lähmungszustände der unteren Extremitäte und deren Behandlung. Stuttgart, 1840. II. Aufl: Spinale Kinderlähmung. Ibidem, 1860.

Higier, H., Zur Klinik der Schweissanomalien bei Poliomyelitis anterior (spinale Kinderlähmung) und posterior (Herpes zoster). Deutsche Zeitschr. f. Nervenheilk., 1901.

Hlava, Poliomyelitis anterior acuta partialiter haemorrhagia. Sbornik lekarsky, 1891.

Hoche, Experimentale Beiträge zur Pathologie des Rückenmarks. Arch. f. Psychiatrie, 1899.

Hochhaus, Über Poliomyelitis acuta. Münchner med. Wochenschr., 1909.

Hoffmann, Aug., Cerebrale und spinale Kinderlähmung bei Geschwistern. Münchner med. Wochenschr., 1904.

Hoffmann, J., Zur Kenntniss der syphilitischen akuten und atrophischen Spinallähmung (Poliomyelitis anterior acuta et chronica syphilitica). Neurol. Centralbl., 1909.

Hoffmann, J., Über eine Epidemie von Poliomyelitis anterior acuta in der Umgebung Heidelbergs im Sommer und Herbst 1908 und bemerkenswerte Beobachtungen aus früheren Jahren. Deutsche Zeitschr. f. Nervenheilk., 1909.

Hohmann, G., Zur Behandlung des Frühstadiums der Poliomyelitis anterior acuta. Münchner med. Wochenschr., 1909.

Holt, L. Emmet, Some clinical features of epidemic poliomyelitis. Archiv. of Pediatrics, 1910.

Huet, E., Un cas de paralysie spinale infantile avec participation du nerf recurrent. Rev. neurol., 1900.

Ibrahim, J., und Hermann, O., Über Bauchmuskellähmung bei Poliomyelitis anterior acuta im Kindesalter. Deutsche Zeitschr. f. Nervenheilk., 1905.

Immermann, Über Poliomyelitis anterior acuta und Landrysche Paralyse. Neurol. Zentralbl., 1885.

Jagic, N., Zur Kenntnis der akuten Poliomyelitis der Erwachsenen. Wiener med. Wochenschr., 1889.

Johannessen, Axel, Bemerkungen über Poliomyelitis anterior acuta. Festschr. f. A. Jacobi. New York, 1900.

Jones, L. A., Infantile paralysis as observed in health district No. 15 during 1909. Monthly Bulletin of the Massachusetts State Board of Health, 1910.

Kady, H., Über die Blutgefässe des menschlichen Rückenmarks. Lemberg, 1889.

v. Kahlden, C., Über Entzündung und Atrophie der Vorderhörner des Rückenmarks. Zieglers Beiträge z. Path. u. path. Anat., 1893.

Kalischer, Über Teleangiektasien mit unilateraler Hypertrophie und über Knochenverlängerung bei spinaler Kinderlähmung. Monatsschr. f. Psych. u. Neurol., 1899.

Kawka, V., Beiträge zur pathologischen Anatomie der spinalen Kinderlähmung. Diss., 1899.

Knoepfelmacher, W., Experimentelle Übertragung der Poliomyelitis anterior acuta auf Affen. Med. Klin., 1909.

Kraus, R., Über das Virus der Poliomyelitis acuta, zugleich ein Beiträg zur Frage der Schutzimpfung. Wiener klin. Wochenschr., 1910.

Krause, P., Zur Kenntnis der westfälischen Epidemie von akuter Kinderlähmung. Deutsche med. Wochenschr., 1909.

Krause, P., Kurze Mitteilung über die rheinisch-westfälische Epidemie von akuter Kinderlähmung. Verh. d. deutsch. Kongr. f. inn. Med., 1910.

Krause and Meinicke, Zur Ätiologie der akuten epidemischen Kinderlähmung. II. Mitteil. Deutsche med. Wochenschr., 1910.

Laborde, J. V., De la paralysie (dite essentielle) de l'enfance. Paris, 1864.

Lamy, Sur un cas d'encéphalite corticale et de poliomyélite antérieur associées. Rev. neurol., 1894.

Landsteiner and Levaditi, La transmission de la paralysie infantile aux singes. Compt. rend. Soc. biol. à Paris, 1909.

Landsteiner and Levaditi, La paralysie infantile expérimentale. Compt. rend. Soc. biol. à Paris, 1909.

Landsteiner and Popper, Übertragung der Poliomyelitis acuta auf Affen. Zeitschr. f. Immunitätsforsch. u. experim. Therapie, 1909.

Landsteiner and Prasek, Übertragung der Poliomyelitis acuta auf Affen. II. Mitteil. Zeitschr. f. Immunitätsforsch. u. experim. Therapie, 4, 1910.

Leegaard, Chr., Beretning on en Epidemi af Poliomyelitis anterior acuta i Bratsberg Amt Aar 1899. Norsk. mag. f. Laegev., 1901.

Leegaard, Chr., Kliniske og Epidemioliske Undersögelser over der akuten Poliomyelit i Norge. Vidensk. Selsk. Skr. Christiania, 1909.

Leiner, K., and v. Wiesner, R., Über epidemische Poliomyelitis. Verhandl. d. deutsch. path. Gesellsch. Erlangen, April, 1910.

Leiner, K., and v. Wiesner, R., Experimentelle Untersuchungen über Poliomyelitis acuta anterior. I–IV. Wiener klin. Wochenschr., 1909–1910.

Leiner, K., and v. Wiesner, R., Experimentelle Untersuchungen über Poliomyelitis acuta in Verhandl. d. 82. Versamml. d. Gesellsch. deutsch. Naturforscher und Arzte in Konigsberg, 1910.

Lentz and Huntemüller, Über akute epidemische Kinderlähmung. Centralbl. f. Bakteriol., 1910.

Leri and Wilson, Un cas de poliomyélite antérieure aïgue de l'adulte avec lésions en foyers. Nouv. iconogr. de la Salp., 1904.

Levaditi, C., and Landsteiner, K., Recherches sur la paralysie infantile expérimentale. Compt. rend. Soc. biol. à Paris, 1909.

Levaditi and Landsteiner, La poliomyélite expérimentale. Compt. rend. Soc. biol. à Paris, 1910.

Levaditi and Landsteiner, Étude expérimentale de la poliomyélite aïgue. Compt. rend. Soc. biol. à Paris, 1910.

Leyden, E., Beiträge zur pathologischen Anatomie der atrophischen Lähmung der Kinder und der Erwachsenen. Arch. f. Psychiatrie, 1876.

Leyden, E., Über Poliomyelitis und Neuritis. Zeitschr. f. klin. Med., 1880.

Lindner und Mally, Zur Poliomyelitisepidemie in Oberösterreich, 1908. Deutsche Zeitschr. f. Nervenheilk., 1910.

Löcker, J., Die Poliomyelitisepidemie im oberösterreichischen Landbez. Steyr. Das österr. Sanitätswesen, 1909.

Lövegren, Ellis, Zur Kenntnis der Poliomyelitis anterior acuta und subacuta s. chronica. Das Jahrb. f. Kinderheilk., 1904.

Lovett, R. W., The occurrence of infantile paralysis in Massachusetts in 1907. Boston Med. and Surg. Journal, 1908.

Lovett, R. W., and Lucas, W. P., A study of six hundred and thirty-five cases of infantile paralysis. Journ. of Amer. Med. Assoc., 1908.

Lovett, R. W., and Emerson, H. C., The occurrence of infantile paralysis in Massachusetts in 1908. Monthly Bulletin of the Massachusetts State Board of Health, 1909.

Machol, Die chirurgisch-orthopädische Behandlung der spinalen Kinderlähmung. Münchner med. Wochenschr., 1910.

Mackenzie, Epidemic poliomyelitis, with the report of ten cases. Med. Rec., 1902.

Macphail, A preliminary note on an epidemic of paralysis in children. Brit. Med. Journ., 1894.

Marburg, Otto, Zur Pathologie der Poliomyelitis acuta. Wiener klin. Rundschau, 1909.

Marchand, Über einen Fall von akuter Poliomyelitis bei einem Erwachsenen. Münchner med. Wochenschr., 1910.

Marie, Pierre, Hémiplégie cérébrale infantile et maladies infectieuses. Progr. méd., 1885.

Marie, Pierre, Leçons sur la maladie de la moelle. Paris, 1892.

Marie, Pierre, La paraplégie cérébrale infantile. Bull. méd., 1902.

Marie, Pierre, Sur la coincidence chez un même malade de la paraplégie cérébrale infantile et de la paralysie spinale infantile. Bull et mém. Soc. méd. des hôpit.

Marinesco, G., Nature et traitement de la myélite aïgue. Nouv. Icon. de la Salp., 1900.

Marie, Pierre, Sur la scoliose tardive dans la paralysie spinale infantile. Internat. Beitr. z. inn. Med. Festschrift f. Leyden. Berlin, 1902.

Matthes, Sektionsbefund bei einer frischen spinalen Kinderlähmung. Deutsche Zeitschr. f. Nervenheilk., 1898.

Medin, O., Über eine Epidemie von spinaler Kinderlähmung. Verhandl. d. x. Internat. Kongr. Berlin, 1890.

Medin, O., Om den infantila paralysien, med sarskild hansyn till dess akuta stadium. Deutsche med. Wochenschr., 1896.

Medin, O., L'état aïgue de la paralysie infantile. Arch. de méd. des enfants, 1898.

Meinicke, E., Experimentelle Untersuchung über akute epidemische Kinderlähmung, 1910. Deutsche med. Wochenschr. Nr. 15, 1910.

Meinicke, E., Praktische Ergebnisse der experimentellen Untersuchungen über akute epidemische Kinderlähmung. Verhandl. d. deutsch. Kongr. f. inn. Med., 1910.

Möbius, in Schmidts Jahrb., 204, 1884, S. 135.

Mönckeberg, J., Anatomischer Befund eines Falles von Landryschen Symptomencomplex. Münchner med. Wochenschr., 1903.

Money, A., The spinal cord of recent and old cases of infantile palsy. Trans. of the Pathol. Soc. London, 1884.

Mott, F. W., Microscopical examination of the spinal cord, peripheral nerves and muscles in a case of acute poliomyelitis. Fatal termination sixteen days from the onset. Arch. of Neurol., 1899.

Müller, Ed., Über die Frühstadien der spinalen Kinderlähmung. Münchner med. Wochenschr., 1909.

Müller, Ed., Die spinale Kinderlähmung. Berlin, 1910.

Müller, Franz, Die akute atrophische Spinallähmung der Erwachsenen. Stuttgart, 1880.

Nannestad, Bretening om en epidemi af poliomyelitis anterior avuta i Hvaler laegedistrict sommeren 1904. Norsk. Mag. f. Laegev, 1906.

Netter, A., Fréquence insolite des poliomyélites en France pendant l'été et l'automne 1909. Bull. et mém. Soc. méd. des hôpit., 1909.

Netter, A., Apparition sous forme epidémique de la paralysie infantile à Paris et sa banlieue en 1909. Bull. de l'acad. de méd., 1910.

Netter, A., Paralysies infantiles á début méningitique. Formes méningitiques de la maladie de Heine-Medin. Bull. et mém. Soc. méd. des hôpit., 1910.

Netter, A., Méningites bénignes d'allure epidémique. Bull. et mém. Soc. méd. des hôpit., 1910.

Netter, A., and Tinel, Des modes de début de la poliomyélite aiguë et en particulièr de ses formes méningitiques. Congrès de l'Association française de pédiatrie, 1910.

Netter and Levaditi, Action microbicide exercée par des malades atteinté de paralysie infantile sur le virus de la poliomyélite aiguë. Compt. rend. Soc. biol. à Paris, 1910.

Neurath, R., Ein Fall von infantiler Hemiplegie, kombiniert mit poliomyelitischer Lähmung des zweiten Beines. Wiener med. Presse, 1900.

Neurath, R., Über seltene Knochendeformitäten nach spinaler Kinderlähmung. Wiener med. Presse, 1901.

Neurath, R., Klinische Studien über Poliomyelitis. Klinische Untersuchungen an 240 Fällen von spinaler Kinderlähmung. Jahrb. f. Kinderheilk., 61, 1905.

Neurath, R., Beiträge zur Anatomie der Poliomyelitis anterior acuta. Arb. a. d. neurol. Inst. a. d. Wiener Univers., 1905.

Neurath, R., Atypische Poliomyelitisfälle. Wiener med. Wochenschr., 1909.

Neurath, R., Erfahrungen während der Poliomyelitsepidemie 1908/09, in Wien. Wiener klin. Wochenschr., 1909.

Newmark, L., A little epidemic of poliomyelitis. Med. News, 1899.

Oppenheim, Zur Encephalitis pontis des Kindesalters, zugleich ein Beitrag zur Symptomatologie der Facialis- und Hypoglossuslähmung. Berliner klin. Wochenschr., 1899.

Oppenheim, H., Lehrbuch der Nervenkrankheiten. 5. Aufl. Berlin, 1908.

Oxholm, Tilfaelde af omtrent samtidig optraedende. Lammelse hos Born. Tidskr. f. prakt. Med., 1887.

Packard, F. A., Acute anterior poliomyelitis occurring simultaneously in a brother and sister. Jour. of Nerv. and Ment. Disease, 1899.

Parrot and Joffroy, Note sur un cas de paralysie infantile. Arch de physiol. norm. et pathol., 1870.

Pasteur, W., An epidemic of infantile paralysis occurring in children of the same family. Trans. of the Clin. Soc., 1897.

Peiper, E., Das Auftreten der spinalen Kinderlähmung (Heine-Medinsche Krankheit.), in Vorpommern. Deutsche med. Wochenschr., 1909.

Petrén, K., Till fragan om poliomyelitens kliniska stallning, dess prognos och therapi. Nord. Tidsskr. f. Therapi., 1909.

Petrén, K., and Ehrenberg, L., Études cliniques sur la poliomyélite aiguë. Nouv. iconogr. de la Salp., 1909.

Pierracini, G., Una epidemia di paralisi atrophica spinale infantile. Sperimentale, 1895.

Pirie, J. Harvey, A case of rapidly fatal acute poliomyelitis in an adult. Rev. of Neurol. and Psychiat. Edinb., 1910.

Platou, E., Nogle oplisninger om en epidemi af poliomyelitis anterior acuta i Aafjorden hosten 1904. Tidsskr. f. d. norske Laegef., 1905.

Pleuss, Anton, Über gehäuftes Vorkommen spinaler Kinderlähmung. Inaug. Diss. Kiel, 1898.

Potpeschnigg, Bakteriologische Untersuchungsergebnisse bei Poliomyelitis (Heine-Medinsche Krankheit.). Wiener klin. Wochenschr., 1909.

Praetorius, E., Zur pathologischen Anatomie der Poliomyelitis anterior acuta infantum. Jahrb. f. Kinderheilk., 1903.

Prevost, J. L., und Vulpian, Observation de paralysie infantile; lésions des muscles et de la moelle. Compt. rend. Soc. biol. à Paris, 1865.

Probst, Über die Folgen der spinalen Kinderlähmung auf die hoher gelegenen Nervenzentren. Wiener klin. Wochenschr., 1898.

Ranken, Nagra fall af "barnforlamning" behandlade med "banande" ofningsterapi. Finska Lakaresallsk. Handl., 1909.

Raymond, F., Paralysie infantile, atrophie musculaire. Compt. rend. Soc. biol., 1875.

Raymond, F., Leçons sur les maladies du système nerveux. 2. Paris, 1897. O. Doin.

Raymond and Sicard, Méningite cérébro-spinale a forme de paralysie infantile, cytodiagnostic. Rev. neurol., 1902.

Redlich, E., Beiträge zur pathologischen Anatomie der Poliomyelitis anterior acuta infantum. Wiener klin. Wochenschr., 1894.

Report of the collective investigation committee on the New York epidemic, epidemic poliomyelitis. Jour. of Nerv. and Ment. Disease, Monograph Series No. 6, 1910.

Rissler, John, Zur Kenntnis der Veränderungen des Nervensystems bei Poliomyelitis anterior acute. Nord. med. Ark., 1888.

Rocaz and Carles. Paralysie infantile des muscles de la paroi abdominale avec pseudohernie ventrale. Arch. de med. des enfants, 1908.

Römer, P. H., Untersuchungen zur Ätiologie der epidemischen Kinderlähmung. Münchner med. Wochenschr., 1906.

Römer, P. H., Weitere Mitteilungen über experimentelle Affenpoliomyelitis. Münchner med. Wochenschr., 1910.

Römer, P. H., Epidemiologische und ätiologische Studien über die spinale Kinderlähmung. Verhandl. d. deutsch Kongr. f. inn. Med., 1910.

Römer, P. H., and Joseph, K., Beitrag zur Natur des Virus der epidemischen Kinderlähmung. Münchner med. Wochenschr., 1910.

Römer and Joseph, Über Immunität und Immunisierung gegen das Virus der epidemischen Kinderlähmung. Münchner med. Wochenschr., 1910.

Römer, P. H., and Joseph, K., Spezifisch wirksames Serum gegen das Virus der epidemischen Kinderlähmung. Münchner med. Wochenschr., 1910.

Römer, P. H., and Joseph, K., Beiträge zur Prophylaxe der epidemischen Kinderlähmung. Münchner med. Wochenschr., 1910.

Römer, P. H., and Joseph, K., Zur Natur und Verbreitungsweise des Poliomyelitisvirus. Münchner med. Wochenschr., 1910.

Roger and Damaschino, Recherches anatomo-pathologiques sur la paralysie spinale de l'enfance. Rev. de méd., 1881.

Roger and Damaschino, Recherches anatomo-pathologiques sur la paralysie spinale de l'enfance. Compt. rend. Soc. biol. à Paris, 1871.

Rossi, Reprises chroniques de poliomyélite aiguë de l'enfance avec apparences de myopathie. Rev. neurol., 1905.

Rossi, Coincidence chez un même malade de la paraplégie cérébrale infantile et de la paralysie spinale infantile. Nouv. iconogr. de la Salp., 1907.

Roth, M., Anatomischer Befund bei spinaler Kinderlähmung. Virchows Archiv, 1873.

Rumpf, Beiträge zur pathologischen Anatomie des zentralen Nervensystems. Arch. f. Psychiatrie, 1885.

Russell, J. Risien, The prognosis and treatment of acute anterior poliomyelitis. Med. Soc. Transac., 1908.

Sahli, Zur Lehre von den spinalen Lokalisationen. Deutsche Arch. f. klin. Med., 1883.

Sander, Über Rückwirkung der spinalen Kinderlähmung auf die motorischen Gebiete der Hirnrinde. Zentralbl. f. d. med. Wiss., 1875.

Schlesinger, H., in Verhandl. der Gesellsch. deutsch. Nervenärzte. III. Jahresvers. Wien, 1909.

Schmaus, Beitrag zur Kasuistik der akuten hämorrhagischen Myelitis, Myelitis bulbi und Landrysche Paralyse. Zieglers Beitr. z. Path. u. path. Anat., 1905.

Schonka, J., Über die Art des Auftretens der infektiosen Poliomyelitis. Das österr. Sanitätswesen, 1909.

Schüller, Drei Fälle poliomyelitischer Lähmung einer unteren Extremität mit positiven Babinski. Neurol. Zentralbl., 1905.

Schultze, Fr., Beiträge zur Pathologie und pathologischen Anatomie des zentralen Nervensystems, insbesondere des Rückenmarks. Virchows Arch., 1876.

Schultze, Fr., Die anatomischen Veränderungen bei der akuten atrophischen Lähmung der Erwachsenen. Virchows Arch., 1878.

Schultze, Fr., Zur Ätiologie der akuten Poliomyelitis. Münchner med. Wochenschr., 1898.

Schultze, Fr., Zur pathologischen Anatomie und Ätiologie der akuten Poliomyelitis und der aufsteigenden (Landryschen Paralyse). Zieglers Beitr. z. Path. u. path. Anat., 1905.

Schwalbe, E., Untersuchung eines Falles von Poliomyelitis acuta infantum im Stadium der Reparation. Zieglers Beitr. z. Path. u. path. Anat., 1902.

Seeligmüller, A., Spinale Kinderlähmung. In Handb. f. Kinderkrankh. herausg. von Gerhardt, 5, 1880.

Seeligmüller, A., Über Lähmungen im Kindesalter. Jahrb. f. Kinderheilk., 1878/1879.

Siemerling, E., Zur pathologischen Anatomie der spinalen Kinderlähmung. Arch. f. Psychiatrie, 26, 1894.

Spieler, Zur Epidemie der Heine-Medinschen Krankheit (Poliomyelitis anterior acuta), in Wien, 1908/09. Wiener med. Wochenschr., 1910.

Stadelmann, E., Beiträge zur Pathologie und pathologischen Anatomie der Rückenmarks-erkrankungen. Deutsch. Arch. f. klin. Med., 1883.

Starr, M. Allen, Epidemic infantile paralysis. Journ. of Amer. Med. Assoc., 1908.

Strassburger, Zur Klinik der Bauchmuskellähmungen auf Grund eines Falles von isolierter partieller Lähmung nach Poliomyelitis anterior acuta. Deutsche Zeitschr. f. Nervenheilkunde, 1906.

Strauss, J., The pathology of acute poliomyelitis. In report of the collective investigation committee, etc. (See above.)

Strümpell, A., Über die Ursachen der Erkrankungen des Nervensystems. Deutsch. Arch. f. klin. Med., 35, 1884.

Strümpell, A., Über die akute Encephalites der Kinder (Polioencephalite acuta, cerebrale Kinderlähmung). Jahrb. f. Kinderheilk., 1885.

Strümpell, A., Zur Ätiologie der spinalen Kinderlähmung (Poliomyelitis acuta). Beitr. z. pathol. Anat. u. klin. Med. Leipzig, 1887.

Strümpell, A., and Barthelmes, Über Poliomyelitis acuta der Erwachsenen und über die Verhältnisse der Poliomyelitis zur Polyneuritis. Deutsche Zeitschr. f. Nervenheilk., 1900.

Takahashi, Y., Ein Fall akut entstandener doppelseitiger Lähmung des äusseren Okulomotorius und Trochlearis. Klin. Monatsbl. f. Augenheilk., 1908.

Taylor, E. W., Poliomyelitis of the adult. Journ. of Nerv. and Ment. Dis., 1902.

Taylor, H. L., Is infantile paralysis epidemic? New York Med. Journ., 1897.

Taylor, M., An epidemic of poliomyelitis. Phila. Med. Journ., 1898.

Tedeschi, E., Paralisi spinale infantile acuta conemiatrofia facciale ed atrofia del nervo ottico. Atti dell' Accademia di Scienze mediche naturali in Ferrara, 1904.

Tiedemann, Poliomyelitis acuta und Meningitis cerebro-spinalis. Münchner med. Wochenschr., 1906.

Triboulet and Lippmann, Poliomyélite antérieure aiguë, ponction lombaire, mononucleose. Bull. et Mem. de la Soc. med., 1902.

Verhandlungen der Gesellschaft deutscher Nervenärzte, 3. Jahresversammlung, Wien, 1909. Deutsche Zeitschr. f. Nervenheilk., 1910.

Vulpius, O., Die Behandlung der spinalen Kinderlähmung. Leipzig, 1910.

Wickman, Ivar, Über die Prognose der akuten Poliomyelitis und atiologisch verwandter Erkrankungen. Zeitschr. f. klin. Med., 1907. Festschr. für S. E. Henschen.

Wickman, Ivar, Studien über Poliomyelitis acuta. Arb. a. d. Path. Inst. d. Universität Helsingfors, 1, 1905. Also separately Berlin, 1905.

Wickman, Ivar, Beiträge zur Heine-Medinschen Krankheit (Poliomyelitis acuta und verwandter Erkrankungen). Berlin, 1907.

Wickman, Ivar, Über die akute Poliomyelitis und verwandter Erkrankungen (Heine-Medinsche Krankheit). Jahrb. f. Kinderheilk., 1908.

Wickman, Ivar, Sur les pretendues relations entre la poliomyélite antérieur aigue et la méningite cérébro-spinale sous forme épidemique. Bull. et mêm. Soc. méd. des hôpit., 1909.

Wickman, Ivar, Weitere Studien über Poliomyelitis acuta. Ein Beitrag zur Kenntnis der Neurophagen und Körnchenzellen. Deutsche Zeitschr. f. Nervenheilk., 1910.

Wickman, Ivar, Über akute Poliomyelitis und Polyneuritis. Zeitschr. f. d. ges. Neurol. u. Psych., 1910.

Wickman, Ivar., in Verhandl. d. 82. Versamml. d. Gesellsch. deutsch. Naturforscher und Ärzte in Königsberg, 1910.

Williams, A case of Strümpell's paralysis (Polio-encephalitis) combined with infantile paralysis. Lancet, 1899.

Wollstein, M., A biological study of the cerebro-spinal fluid in anterior poliomyelitis. Journ. of Exper. Med., 1908.

Zappert, J., Klinische Studien über Poliomyelitis. Jahrb. f. Kinderheilk., 1901.

Zappert, J., Bemerkungen über die derzeitigen Poliomyelitisepidemien in Wien und Umgebung. Wiener med. Wochenschr., 1909.

Zappert, J., Die Epidemie der Heine-Medinschen Krankheit (Poliomyelitis) von 1908 in Wien und Niederösterreich. Wiener med. Wochenschr., 1909.

Zappert, J., Die Epidemie der Poliomyelitis acuta epidemica (Heine-Medinsche Krankheit) in Wien und Niederösterreich im Jahre 1908. Jahrb. f. Kinderheilk., 1910.

Zappert, J., Organische Erkrankungen des Nervensystems. In Pfaundler und Schlossmann, Handb. f. Kinderheilk., 4, 2 Aufl., 1910.

Zappert, J., Heine-Medinsche Krankheit, in Verhandl. d. 82 Versamml. d. Gesellsch. f. deutsche Naturforscher und Ärzte in Königsberg, 1910.

# The Journal

OF

# Nervous and Mental Disease

OFFICIAL ORGAN OF

The American Neurological Association
The New York Neurological Society
Boston Society of Psychiatry and Neurology
The Philadelphia Neurological Society, and
The Chicago Neurological Society

---

*MANAGING EDITOR AND PUBLISHER*
Dr. SMITH ELY JELLIFFE
64 West 56th Street, New York City

*EDITOR*
Dr. WILLIAM G. SPILLER

*ASSOCIATE EDITORS*
Dr. E. W. TAYLOR
Dr. E. E. SOUTHARD

*ADVISORY BOARD OF EDITORS*

Dr. WM. OSLER
Dr. CHARLES L. DANA
Dr. F. X. DERCUM
Dr. CHAS. K. MILLS
Dr. M. ALLEN STARR
Dr. ADOLF MEYER
Dr. HUGH T. PATRICK
Dr. JAS. PUTNAM
Dr. B. SACHS
Dr. WHARTON SINKLER
Dr. FEDERICK PETERSON
Dr. WILLIAM A. WHITE

*FOREIGN AND DOMESTIC AGENTS*

S. Karger, Karlstrasse 15, Berlin, Germany; H. K. Lewis, 136 Gower Street, London W. C.; Steiger & Co., 25 Park Place, New York; Gustave E. Stechert, 129 West 20th Street, New York; Paul B. Hoeber, 69 East 57th Street, New York.

Printed by The New Era Printing Company, Lancaster, Pa.

*ISSUED MONTHLY—50 Cents Per Copy—$5.00 PER YEAR*
*Foreign Subscription, 5.60 per Year.*

## NERVOUS AND MENTAL DISEASE MONOGRAPH SERIES

Edited by

Drs. SMITH ELY JELLIFFE and WM. A. WHITE

Numbers Issued

1. Outlines of Psychiatry. (4th Edition.) $3.00.
By Dr. William A. White.
2. Studies in Paranoia.
By Drs. N. Gierlich and M. Friedman.
3. The Psychology of Dementia Praecox. (Out of Print.)
By Dr. C. G. Jung.
4. Selected Papers on Hysteria and other Psychoneuroses.
(2d Edition.) $2.50. By Prof. Sigmund Freud.
5. The Wassermann Serum Diagnosis in Psychiatry. $2.00.
By Dr. Felix Plaut.
6. Epidemic Poliomyelitis. New York, 1907. (Out of Print.)
7. Three Contributions to Sexual Theory. $2.00.
By Prof. Sigmund Freud.
8. Mental Mechanisms. $2.00. By Dr. Wm. A. White.
9. Studies in Psychiatry. $2.00.
New York Psychiatrical Society.
10. Handbook of Mental Examination Methods. $2.00.
By Shepherd Ivory Franz.
11. The Theory of Schizophrenic Negativism. $0.60.
By Professor E. Bleuler.
12. Cerebellar Functions. $3.00.
By Dr. André-Thomas.
13. History of Prison Psychoses. $1.25.
By Drs. P. Nitsche and K. Wilmanns.
14. General Paresis. $3.00. By Prof. E. Kraepelin.
15. Dreams and Myths. $2.00. By Dr. Karl Abraham.
16. Poliomyelitis. $3.00. Dr. I. Wickmann.
17. Freud's Theories of the Neuroses. $2.00.
Dr. E. Hitschmann.